touch™ ONCOLOGY

Adverse event identification and management in locally advanced/metastatic urothelial carcinoma

Practice aid for the management of adverse events of special interest in the use of immunotherapies and targeted therapies

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Antibody–drug conjugate

Enfortumab vedotin[1,2]

Adverse event	Monitoring regimen	Actions

 **PERIPHERAL NEUROPATHY**	• Review systems and conduct passive and active physical assessments, including musculoskeletal and neurologic examinations	• Grade 2: Withhold until grade ≤1
		  • First occurrence: Resume treatment at the same dose level
		  • Recurrence: Withhold until grade ≤1, and then resume treatment reduced by one dose level*
		• Grade ≥3: Permanently discontinue

 **OCULAR**	• Consider baseline and routine eye examinations for patients with known ocular disorders • Patient reporting of ocular problems should prompt action	• Artificial tears can prevent dry eyes and reflexive tearing • Wearing spectacles while on treatment may reduce risk of keratitis associated with contact lens use • Consider referral for ophthalmologic evaluation if ocular symptoms do not resolve or worsen
 **HYPERGLYCAEMIA**	• Assess baseline HbA1c before starting treatment • Routine monitoring of non-fasting blood glucose levels prior to each dose	• Withhold until blood glucose ≤13.9 mmol/L (≤250 mg/dL) • Resume treatment at the same dose level
 **SKIN REACTIONS**	• Thorough assessment for the presence and extent of reactions starting at treatment initiation • Frequent and thorough follow-up, including monitoring for secondary skin infections	• Mild to moderate skin reactions: Topical corticosteroids or antihistamines • Suspected SJS, TEN or bullous lesions: Immediately withhold and refer to specialized care • Grade 2 worsening/with fever or grade 3: Withhold until grade ≤1; consider referral to specialist care; resume at same/lower dose level* • Confirmed SJS or TEN; Grade 4 or recurrent grade 3: Permanently discontinue

*Refer to product information for details of recommended dose reductions.

Antibody–drug conjugate

Sacituzumab govitecan[3]

Adverse event	Monitoring regimen	Actions
 **DIARRHOEA**	• Patient-reported symptoms • Monitor patients with diarrhoea	• Give fluid and electrolytes, as clinically indicated • At onset of diarrhoea, evaluate for infectious causes and, if negative, initiate loperamide • Grade 3–4: Withhold until resolved to grade ≤1 and reduce subsequent doses* • Patients with an excessive cholinergic response may require premedication (e.g. atropine) with subsequent treatments
 **NAUSEA AND VOMITING**	• Patient-reported nausea and vomiting while receiving treatment • Monitor for uncontrolled nausea and vomiting	• Premedicate with a two- or three-drug combination regimen, e.g. dexamethasone with either 5-HT3 receptor antagonist or NK_1 receptor antagonist • Grade 3 nausea or grade 3/4 vomiting at time of scheduled treatment administration: Withhold until grade ≤1 and resume with additional supportive measures • Additional antiemetics and other supportive measures may also be employed as clinically indicated.
 **HYPERSENSITIVITY**	• Close observation for infusion-related reactions during each infusion and for at least 30 minutes after completion of infusion	• Pre-infusion treatment, including antipyretics, H_1 and H_2 blockers, is recommended; corticosteroids for patients with prior infusion reactions • Slow or interrupt infusion if the patient develops an infusion-related reaction • Permanently discontinue if life-threatening infusion-related reactions occur
 **NEUTROPENIA**	• Patient-reported fever, chills or other signs of infection • Monitor blood cell counts periodically during treatment	• Withhold if absolute neutrophil count below 1,500/mm^3 on day 1 of any cycle or neutrophil count below 1,000/mm^3 on day 8 of any cycle • Withhold if febrile neutropenia and initiate anti-infective treatment • Dose reductions or discontinuation may be considered* • Consider G-CSF for secondary prophylaxis

*Refer to product information for details of recommended dose reductions.

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FGFR inhibitor

Erdafitinib[4]

Adverse event	Monitoring regimen	Actions

 **CSR/RPED**	• Decreased visual acuity or lines of vision from baseline
	• Ophthalmologic examinations monthly for first 4 months, then every 3 months, or urgently if visual symptoms occur, to include:
	  • Assessment of visual acuity
	  • Slit lamp examination
	  • Fundoscopy
	  • Optical coherence tomography
		• Grade 1: Withhold until resolution; if resolves within 4 weeks, resume at the next lower dose level; if no recurrence for a month, consider re-escalation*
		• Grade 2: Withhold until resolution; if resolves within 4 weeks, resume at next lower dose level*
		• Grade 3: Withhold until resolution; if resolves within 4 weeks, resume at next two dose levels lower*
		  • If recurs, consider permanent discontinuation
		• Grade 4: Permanently discontinue

 **HYPERPHOSPHATAEMIA**	• Assess serum phosphate level between 14 and 21 days of initiating treatment • Monthly phosphate level monitoring throughout treatment	• Dietary phosphate restriction for all patients (600–800 mg daily) • If serum phosphate >7.0 mg/dL, assess weekly and consider an oral phosphate binder until <5.5 mg/dL • 5.6–6.9 mg/dL: Continue at current dose • 7.0–9.0 mg/dL: Withhold until <5.5 mg/dL; resume at same dose level (consider dose reduction if hyperphosphataemia for >1 week) • >9.0 mg/dL: Withhold until <5.5 mg/dL; resume at 1 dose level lower* • >10.0 mg/dL, significant alteration in baseline renal function or grade 3 hypercalcaemia: Withhold until <5.5 mg/dL; resume at 2 dose levels lower*
 **NAIL/SKIN REACTIONS**	• Patient-reported progressive or intolerable skin or nail disorders	• Grade 3: Withhold until grade ≤1; resume at next lower dose level* • Grade 4: Permanently discontinue

*Refer to product information for details of recommended dose reductions.

Immune checkpoint inhibitors

Atezolizumab,[5] avelumab,[6] nivolumab[7] and pembrolizumab[8]

Adverse event	Monitoring regimen	Actions
 **COLITIS**	• Monitor for signs and symptoms • Rule out causes other than immune-related colitis	• Grade ≥2: Corticosteroids should be administered* • Grade 2/3 colitis or diarrhoea: Withhold until grade ≤1 • Recurrent grade 3 colitis: Permanently discontinue (avelumab and pembrolizumab) • Grade 4 colitis or diarrhoea: Permanently discontinue
 **HEPATITIS**	• Monitor ALT, AST and bilirubin prior to initiation of treatment, periodically during treatment and as indicated based on clinical evaluation	• Grade ≥2: Corticosteroids should be administered* • Grade 2, ALT or AST >3 to 5 times ULN or blood bilirubin >1.5 to 3 times ULN: Withhold until grade ≤1 • Grade 3/4, ALT or AST >5 times ULN or blood bilirubin >3 times ULN: Permanently discontinue

 **NEPHRITIS**	• Monitor for elevated serum creatinine prior to and periodically during treatment	• Grade ≥2: Corticosteroid therapy should be administered*
		• Grade 2, serum creatinine >1.5 to ≤3 times ULN: withhold until grade ≤1
		• Grade 3, serum creatinine >3 to ≤6 times ULN:
		  • Withhold until grade ≤1 (avelumab and nivolumab)
		  • Permanently discontinue (atezolizumab and pembrolizumab)
		• Grade 4, serum creatinine >6 times ULN: Permanently discontinue

*Refer to product information for recommendations on corticosteroid use and tapering before resuming treatment.

Immune checkpoint inhibitors

Atezolizumab,[5] avelumab,[6] nivolumab[7] and pembrolizumab[8]

Adverse event	Monitoring regimen	Actions
 **PNEUMONITIS**	• Monitor for signs and symptoms • Rule out causes other than immune-related pneumonitis	• Grade ≥2: Corticosteroids should be administered* • Grade 2: Withhold until grade ≤1 • Recurrent grade 2: Permanently discontinue (avelumab and pembrolizumab) • Grade 3/4: Permanently discontinue

 **HYPOTHYROIDISM or HYPERTHYROIDISM**	• Monitor for signs and symptoms
	• Monitor for changes in thyroid function at start of treatment, periodically during treatment and as indicated based on clinical evaluation
		• **Hypothyroidism**: withhold until symptoms are controlled by thyroid replacement therapy and TSH levels are decreasing
		  • No treatment interruption needed with pembrolizumab
		  • Permanently discontinue nivolumab if grade 4
		• **Hyperthyroidism**: Treatment may be resumed when symptoms are controlled by antithyroid medication and thyroid function is improving
		  • Withhold pembrolizumab until grade ≤1 or grade ≤2 controlled with antithyroid medication and after steroid taper; otherwise, discontinue
		  • Withhold avelumab if grade 3/4 until grade ≤1
		  • Permanently discontinue nivolumab if grade 4

*Refer to product information for recommendations on corticosteroid use and tapering before resuming treatment.

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Abbreviations and references

Abbreviations

5-HT3, 5-hydroxytryptamine 3; ALT, alanine transaminase; AST, aspartate transaminase; CSR/RPED, central serous retinopathy/retinal pigment epithelial detachment; FGFR, fibroblast growth factor receptor; G-CSF, granulocyte-colony stimulating factor; HbA1c, haemoglobin A1c; NK_1, neurokinin-1; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis; TSH, thyroid-stimulating hormone; ULN, upper limit of normal.

References

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