

Systemic Anti Cancer Therapy Protocol

Atezolizumab For Urinary tract squamous cell carcinoma (Compassionate use)

PROTOCOL REF: MPHAAUTSCC
(Version No.: 1.0)

Approved for use in:

Palliative second line treatment for urinary tract squamous cell carcinoma, which is PDL1 positive, following first line palliative platinum combination chemotherapy. **This funding applies for a single patient under the care of Dr. J Chan.**

Dosage:

Drug	Dosage	Route	Frequency	Duration of Treatment
Atezolizumab	1200mg (Flat dose)	IV Infusion	3 weekly	Until disease progression or unacceptable toxicity

Exclusions

History of pneumonitis, organ transplantation, HIV infection, active hepatitis B or C infection

Active infection requiring systemic treatment

Less than 4 weeks from major surgery

History of clinically severe autoimmune disease

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Supportive Therapy:

Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Atezolizumab is a monoclonal antibody- considered to be neutral.

Refer to the CCC policy for the '[Prevention and Management of Extravasation Injuries](#)'.

Dosing in renal and hepatic impairment (Prior to start of treatment ONLY/Baseline):

Renal	Atezolizumab	GFR \geq 30ml/min- proceed with treatment GFR < 30ml/min- limited data use with caution
Hepatic	Atezolizumab	Administered with caution in patients with: Moderate (total bilirubin > 1.5 -3 x ULN and any AST) or Severe (total bilirubin > 3 x ULN and any AST*) hepatic impairment. * Within normal limits or high

Patient Counselling Points

Women of childbearing potential should use effective contraception throughout treatment and for at least 5 months following the last dose of atezolizumab.

Contact the triage team for the following:

- New or worsening cough, chest pain or shortness of breath
- Diarrhoea or severe abdominal pain (with or without blood/mucous)
- Jaundice, severe nausea or vomiting, or easy bruising or bleeding
- Persistent or unusual headache, extreme weakness, dizziness or fainting, or vision changes
- Monitor for signs of infection / sepsis

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Interactions:

No formal pharmacokinetic drug interaction studies have been conducted with atezolizumab. Since atezolizumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.

Please consult [SmPC](#) for full information on interactions.

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Sodium chloride 0.9%	250mL	IV	Flush
1	Atezolizumab	1200mg	IV	250mL sodium chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30minutes in a non-pyrogenic line with a 0.2 micron filter

Repeated every 3 weeks until disease progression or unacceptable toxicity.

Routine prophylaxis against infusion related reactions is not required. However, monitor during the infusion and treatment given if necessary (antihistamines, steroids etc.).

Please refer to the CCC [Hypersensitivity; Management Prevention Policy](#)

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Main Toxicities:

For full details on assessment and management of immune-related toxicities refer to [CCC Immuno-Oncology toxicity specific guidance for adverse event management](#).

Immune related toxicities	
<p>Immune-Mediated Pneumonitis</p> <p>Pneumonitis occurred in 3% of melanoma patients (including G3 in 0.2%).</p>	<p>Monitor patients for signs and symptoms and evaluate with radiographic imaging and administer corticosteroids for toxicities of grade 2 or above.</p>
<p>Immune-Mediated Colitis</p>	<p>Monitor patients for signs and symptoms and administer corticosteroids for grade 2 or greater.</p>
<p>Other Immune-Mediated Toxicities:</p> <p>Hepatitis Hypophysitis Nephritis Hyperthyroidism or Hypothyroidism</p> <p>Less frequently: Exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, haemolytic anaemia, Guillain-Barré syndrome</p>	<p>Monitor LFTs, biochemistry, cortisol, TFTs and blood glucose, consider corticosteroids for grade 2 or greater.</p>
<p>Other non-immune adverse events:</p> <p>Fatigue, anaemia Cough, dyspnoea Nausea, decreased appetite Pruritis, rash Constipation, diarrhoea Arthralgia</p>	<p>Symptomatic management for grade 1 with close monitoring</p>
<p>Laboratory abnormalities:</p> <p>Hyponatraemia, hypocalcaemia, hyperglycaemia, hypertriglyceridaemia</p>	<p>Monitor at each cycle and rule out immune-mediated reaction</p>

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Investigations and treatment plan:

If suspicion of endocrinopathies: request TSH, T4, T3, ACTH, cortisol, LH, FSH, testosterone (men) and prolactin (women)

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	x				
Clinical Assessment	x		x		Then every 12 weeks or as clinically indicated
SACT Assessment (to include PS and toxicities)	x	x	x	x	Every cycle
OTR/ Go-ahead	x		x	x	Every cycle
Immunotherapy bloods as per Meditech order set: FBC, U&E/renal profile, Magnesium, LFTs (ALT, AST and Bilirubin), TFTs, cortisol, blood glucose, LDH, CRP	x	x	x	x	Every cycle
Lipid profile (cholesterol)	x				At baseline then if clinically indicated

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Fatigue profile as per Meditech order set: B12, folate, Iron profile, vitamin D, Zinc, Testosterone (men only), ESR	x				At baseline then if clinically indicated
Full set of observations (<i>BP, heart rate, temperature, respiratory rate and O₂ sats</i>)	x	x	x	x	Every cycle
Creatinine Clearance (Cockcroft and Gault)	x				Every cycle only if baseline CrCL <40ml/min or creatinine increases above 1.5x upper limit of normal and baseline
CT scan	x				Every 12 weeks or as clinically indicated
Trop-T, CK, pro-BNP	x				At baseline for all Renal and Melanoma and thereafter as clinically indicated (ECG to be reviewed by clinical team)
ECG	x				
Weight recorded	x	x	x	x	Every cycle
Height recorded	x				

Pregnancy test if applicable.

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Dose Modifications and Toxicity Management:

- Dosing delay or discontinuation may be required based on individual safety and tolerability.
- Guidelines for permanent discontinuation or withholding of doses are contained in dose modifications.
- Detailed guidelines for the management of immune-related adverse reactions are provided in the [CCC Immuno-Oncology toxicity specific guidance for adverse event management](#).

Treatment Threshold

Administer treatment on day 1 if:

Platelets	Neutrophils	Serum Creatinine	Bilirubin	AST/ALT	Alkaline Phosphatase	TSH and Free T4
$\geq 75 \times 10^9/L$	$\geq 1.0 \times 10^9/L$	≥ 1.5 ULN or baseline	$<3 \times$ ULN	$<5 \times$ ULN	$<5 \times$ ULN	Within range or no change from base line

ULN = upper limit of normal

Platelets must be within normal range prior to Cycle 1.

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Toxicity management:

Detailed guidelines are provided in the CCC clinical network immunotherapy acute oncology guidelines. Systemic high-dose corticosteroid with or without additional immunosuppressive therapy may be required for management of severe immune-related adverse reactions.

Toxicity Grade	Action
Grade 1 Mild	Continue treatment increase monitoring and provide symptomatic treatment.
Grade 2 Moderate	Withhold treatment until resolved to \leq grade 1. Refer to Immuno-Oncology toxicity specific guidance for adverse event management.
Grade 3 and Grade 4 Severe	Withhold treatment. Treatment will be permanently discontinued for any unresolving grade 3-4, severe or life-threatening adverse reaction at the treating clinician's discretion. Refer to Immuno-Oncology toxicity specific guidance for adverse event management.

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References:

Attalla K, Haines K, Labow D, Mehrazin R. Squamous Cell Carcinoma of the Renal Pelvis: Atypical Presentation of a Rare Malignancy. *Urol Case Rep.* 2017 May 19;13:137-139. doi: 10.1016/j.eucr.2017.04.007.

Berz D, Rizack T, Weitzen S, Mega A, Renzulli J, Colvin G. Survival of patients with squamous cell malignancies of the upper urinary tract. *Clin Med Insights Oncol.* 2012;6:11-8. doi: 10.4137/CMO.S8103.

Osenberg JE, Hoffman-Censits J, Powles T, van der Heijden MS, Balar AV, Necchi A, Dawson N, O'Donnell PH, Balmanoukian A, Loriot Y, Srinivas S, Retz MM, Grivas P, Joseph RW, Galsky MD, Fleming MT, Petrylak DP, Perez-Gracia JL, Burris HA, Castellano D, Canil C, Bellmunt J, Bajorin D, Nickles D, Bourgon R, Frampton GM, Cui N, Mariathasan S, Abidoye O, Fine GD, Dreicer R. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial. *Lancet.* 2016 May 7;387(10031):1909-20. doi: 10.1016/S0140-6736(16)00561-4.

Powles T, Durán I, van der Heijden MS, Loriot Y, Vogelzang NJ, De Giorgi U, Oudard S, Retz MM, Castellano D, Bamias A, Fléchon A, Gravis G, Hussain S, Takano T, Leng N, Kadel EE 3rd, Banchereau R, Hegde PS, Mariathasan S, Cui N, Shen X, Derleth CL, Green MC, Ravaud A. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. *Lancet.* 2018 Feb 24;391(10122):748-757. doi: 10.1016/S0140-6736(17)33297-X.

Tecentriq 1,200 mg concentrate for solution for infusion, Summary of Product Characteristics, Roche products Limited. Available from www.medicines.org.uk/emc/medicine. Last updated 23rd March 2021

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Circulation/Dissemination

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Version History

Date	Version	Author name and designation	Summary of main changes
26 th October 2021	1.0	Rachel Pritchard Urology SRG Pharmacist	New Regimen Protocol V1.0

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