Atezolizumab

Indication

Locally advanced or metastatic urothelial carcinoma (UC):

- After platinum-containing therapy, or
- In patients who are considered platinum ineligible and whose tumours have a PD-L1 expression ≥5%

Locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy

Untreated PD-L1 positive metastatic non-small cell lung cancer (NSCLC)

Adjuvant treatment following complete resection for adult patients with Stage II to IIIA (7th edition of the UICC/AJCC-staging system) non-small cell lung cancer (NSCLC) whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and whose disease has not progressed following platinum-based adjuvant chemotherapy

Regimen details

3-weekly regimen:
Atezolizumab 1200mg in 250ml 0.9% sodium chloride

4-weekly regimen:
Atezolizumab 1680mg in 250ml 0.9% sodium chloride

Cycle frequency

3 or 4 weekly

Number of cycles

Depends on indication

For adjuvant NSCLC, treat for 1 year (equivalent to a maximum of 13 x 4-weekly cycles)

For previously treated NSCLC, treat for 2 years (equivalent to 26 x 4-weekly cycles)

For untreated NSCLC, there is no stopping rule, treat until disease progression or unacceptable toxicity

For previously treated UC, treat for 2 years (equivalent to 26 x 4-weekly cycles)

For 1st line UC (patients who are ineligible for cisplatin-based chemotherapy), there is no stopping rule, treat until disease progression or unacceptable toxicity

Administration

Atezolizumab is administered in 250mL sodium chloride 0.9% over 60 minutes. If the initial infusion is well tolerated, subsequent infusions may be administered over 30 minutes.

Patients should be monitored (blood pressure, pulse and temperature) every 30 minutes during the infusion for infusion related reactions. For grade 1-2 infusion related reactions, decrease the infusion rate and closely monitor or temporarily interrupt treatment. Premedication with paracetamol and chlorphenamine should be used for further doses and patient should be closely monitored. For grade 3-4 infusion related reactions discontinue treatment.

Pre-medication

None

Emetogenicity

Minimal

Additional supportive medication

None

Extravasation

Neutral

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Thyroid	14 days
Calcium	14 days
Glucose	14 days
Cortisol	14 days
Luteinizing hormone	14 days
Follicle stimulating hormone	14 days
Testosterone	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), Calcium (as indicated), Thyroid (every other cycle)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 75 x 10^9/L
Haemoglobin	≥ 90 g/L
Creatinine	≤ 1.5 x ULN
Bilirubin	≤ 1.5 x ULN
AST	≤ 3 x ULN

Dose modifications

Do not modify atezolizumab dose

Important:
For management of toxicities, consult network Immune Related Toxicity Management Guidelines and see table below

Adverse reaction	Severity	Treatment Modification	
Pneumonitis	Grade 2	Withhold atezolizumab Start 1-2mg/kg methylprednisolone or equivalent Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg oral prednisone equivalent per day.	
	Grade 3 or 4	Permanently discontinue atezolizumab Start 1-2mg/kg methylprednisolone or equivalent	
Hepatitis	Grade 2: (ALT or AST >3-5x upper limit of normal [ULN] or blood bilirubin >1.5−3x ULN)	If persists > 5-7 days, withhold atezolizumab Start 1-2mg/kg methylprednisolone or equivalent Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks and corticosteroids 1-2 mg/kg have been reduced to ≤ 10 mg oral prednisone or equivalent per day	
	Grade 3 or 4: (ALT or AST >5x ULN or blood bilirubin >3x ULN)	Permanently discontinue atezolizumab Start 1-2mg/kg methylprednisolone or equivalent	
Colitis	Grade 2 or 3 Diarrhoea (increase of ≥4 stools/day over baseline) or Symptomatic Colitis	Withhold atezolizumab Start 1-2mg/kg methylprednisolone or equivalent Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg oral prednisone equivalent per day	
	Grade 4 Diarrhoea or Colitis (life threatening; urgent intervention indicated)	Permanently discontinue atezolizumab Start 1-2mg/kg methylprednisolone or equivalent	
Hypothyroidism or hyperthyroidism	Symptomatic	Hypothyroidism: If asymptomatic can receive atezolizumab If symptomatic, withhold treatment and initiate thyroid hormone replacement as needed. Treatment may be resumed when symptoms are	

		controlled by thyroid replacement therapy and TSH levels are decreasing Hyperthyroidism: if asymptomatic can receive atezolizumab If symptomatic, withhold treatment and initiate anti hyperthyroid medication as needed. Treatment may be resumed when symptoms are controlled by methimazole or equivalent and thyroid function is improving
Adrenal insufficiency	Symptomatic	Withhold atezolizumab Start 1-2mg/kg methylprednisolone or equivalent Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to the equivalent of ≤ 10 mg oral prednisone or equivalent per day and patient is stable on replacement therapy
Type 1 diabetes mellitus	Grade 3 or 4 hyperglycaemia (fasting glucose >250-500 mg/dL)	Withhold atezolizumab Treatment may be resumed when metabolic control is achieved on insulin replacement therapy
Infusion-related reactions	Grade 1	Reduce infusion rate to half Once the event has resolved, wait for 30 min while delivering the infusion at the reduced rate. If tolerated, the infusion rate may then be increased to original rate
	Grade 2	Withhold atezolizumab Restart at half of the infusion rate only after the symptoms have resolved
	Grade 3 or 4	Permanently discontinue atezolizumab
Rash	Grade 3	Withhold atezolizumab Start 1-2mg/kg methylprednisolone or equivalent Treatment may be resumed when rash is resolved and corticosteroids have been reduced to ≤ 10 mg oral prednisone equivalent per day
	Grade 4	Permanently discontinue atezolizumab Start 1-2mg/kg methylprednisolone or equivalent

Myasthenic syndrome / myasthenia gravis, Guillain-Barré syndrome and Meningoencephalitis	All Grades	Permanently discontinue atezolizumab Start 1-2mg/kg methylprednisolone or equivalent
Pancreatitis	Grade 3 or 4 serum amylase or lipase levels increased (> 2x ULN) or Grade 2 or 3 pancreatitis	Withhold atezolizumab Start 1-2mg/kg methylprednisolone or equivalent, once symptoms resolved follow with 1-2mg/kg oral prednisolone Treatment with atezolizumab may be resumed when serum amylase and lipase levels improve to Grade 0 or Grade 1 within 12 weeks, or symptoms of pancreatitis have resolved, and corticosteroids have been reduced to ≤ 10 mg oral prednisone or equivalent per day
	Grade 4 or any grade of recurrent pancreatitis	Permanently discontinue atezolizumab Start 1-2mg/kg methylprednisolone or equivalent

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Immune reactions
Interstitial lung disease, pneumonitis
Pancreatitis
Hepatitis
Colitis
Neuropathies
Endocrinopathies

- **Frequently occurring side effects**

Thrombocytopenia
Hypothyroidism, hyperthyroidism
Hypotension
Dyspnoea
Nausea, vomiting
Diarrhoea
Rash
Pruritis
Arthralgia
Fatigue
Infusion related reactions

- **Other side effects**

Decreased appetite
Altered electrolytes
Raised transaminases

Guillain-Barre syndrome

Significant drug interactions

– for full details consult product literature/ reference texts

No formal drug interaction studies have been carried out with atezolizumab.

Corticosteroids: the use of systemic corticosteroids or immunosuppressants before starting atezolizumab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of atezolizumab. However, systemic corticosteroids or other immunosuppressants can be used to treat immunerelated adverse reactions after starting atezolizumab

Additional comments

References

SWAG cancer alliance protocol: https://www.swagcanceralliance.nhs.uk/wp-content/uploads/2020/09/Atezolizumab-v1.1.pdf

Tecentriq SPC: https://www.medicines.org.uk/emc/product/8442/smpc

THIS PROTOCOL HAS BEEN DIRECTED BY DR BIRTLE, DESIGNATED LEAD CLINICIAN FOR BLADDER CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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