ATEZOLIZUMAB (Tecentriq) BEVACIZUMAB

INDICATION (ICD10) C22

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (ATE8)

1. Atezolizumab in combination with bevacizumab for the first-line systemic treatment (not received any systemic therapy) of adult patients with locally advanced or metastatic unresectable hepatocellular carcinoma with Child-Pugh A liver function. Has no symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA666)

REGIMEN SC

(atezolizumab and bevacizumab can be given in any order)

Day 1	ATEZOLIZUMAB	1875mg SC
	BEVACIZUMAB	15mg/kg in #ml sodium chloride 0.9% IV infusion

REGIMEN IV

(atezolizumab and bevacizumab can be given in any order)

Day 1	ATEZOLIZUMAB	1200mg in #ml sodium chloride 0.9% IV infusion
	BEVACIZUMAB	15mg/kg in #ml sodium chloride 0.9% IV infusion

diluent and diluent volume for dose prescribed as per national standardised product specification

Atezolizumab 1200mg IV – The initial dose should be delivered over 60 minutes.
If the first infusion is tolerated without infusion-associated adverse events, the second infusion may be delivered over 30 minutes.
If the 30 minute infusion is well tolerated, all subsequent infusions may be delivered over 30 minutes.

Bevacizumab - The initial dose should be administered over 90 minutes, if tolerated well the second infusion may be administered over 60 minutes.
If the 60 minute infusion is well tolerated all subsequent infusions may be administered over 30 minutes.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days until disease progression.
A formal medical review as to how treatment with atezolizumab in combination with bevacizumab is being tolerated and whether treatment with the combination should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment.

ANTI-EMETICS

Low risk day 1

CONCURRENT MEDICATION REQUIRED

None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Atezolizumab IV – neutral
Bevacizumab – neutral

Atezolizumab IV use of 0.2-5micron filter is optional
Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs, creatinine day 1
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥75
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.
Thyroid function baseline, then every cycle
Random cortisol baseline, then every cycle
Random glucose every cycle
Blood pressure every cycle
Urinalysis for proteinuria every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Atezolizumab	Immune mediated pneumonitis Immune mediated hepatitis Immune mediated colitis Immune mediated endocrinopathies
Bevacizumab	Arterial thromboembolism Gastrointestinal perforation Haemorrhage Hypertension Wound healing complications

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Bevacizumab	Many interactions check carefully

DOSE MODIFICATIONS

Non-haematological

Atezolizumab
Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline
If the drug-related toxicity does not resolve to grade 0-1 within 12 weeks after onset of toxicity, discontinuation is recommended.

Bevacizumab
Hypertension
Baseline blood pressure should be <150/100mmHg.

Diastolic increase >20mmHg above baseline or BP rises to >150/100mmHg	Antihypertensive therapy may be required.
Blood pressure >180/110mmHg	It is advised that bevacizumab therapy is withheld until blood pressure controlled.

Proteinuria
Patients with a history of hypertension may be at increased risk for the development of proteinuria when treated with bevacizumab. There is evidence suggesting that all grade proteinuria may be related to the dose.
Monitoring of proteinuria by dipstick urinalysis is recommended prior to starting and during therapy. Grade 4 proteinuria (nephrotic syndrome) was seen in up to 1.4% of patients treated with bevacizumab. Therapy should be permanently discontinued in patients who develop nephrotic syndrome.

Wound healing
Bevacizumab may adversely affect the wound healing process. Therapy should not be initiated for at least 28 days following major surgery or until the surgical wound is fully healed. Therapy should also be withheld for at least 28–60 days before elective surgery.

REFERENCES

1. Finn, R et al; NEJM 2020; 382: 1894-1905