AVELUMAB AXITINIB (Bavencio, Inlyta)

INDICATION (ICD10) C64

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (AVE3)

1. Avelumab axitinib in treatment-naïve patients (or has received prior systemic therapy in the context of adjuvant/neoadjuvant therapy, which was completed ≥12 months previously) with unresectable locally advanced or metastatic, favourable risk, renal cell carcinoma. Risk status as assessed by the International Metastatic RCC Database Consortium (IMDC) system for this patient is FAVOURABLE-RISK (ie no risk factors present, and therefore an IMDC score of zero). Note: The combination of avelumab and axitinib CANNOT be used for patients who have an IMDC risk status of intermediate or poor. No symptomatic brain metastases or leptomeningeal metastases currently requiring steroids for symptom control. PS 0 or 1. (TA645)

REGIMEN

Day 1	Premedication 30 minutes prior to infusion (see concurrent medication):	
	Chlorphenamine	10mg IV bolus
	Paracetamol	1000mg tablet
	AVELUMAB	800mg in 250ml sodium chloride IV infusion over 60 minutes
Days 1 to 14	AXITINIB	5mg oral twice daily continuously

ADMINISTRATION

Axitinib
Available as 1mg, 3mg, 5mg and 7mg tablets
Swallow whole with or without food.
Grapefruit and grapefruit juice should be avoided while on axitinib.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days
A medical review as to whether treatment with avelumab should continue or not will need to occur at least by the end of the first 8 weeks of treatment.
To be treated until loss of clinical benefit or excessive toxicity or patient choice, whichever is the sooner. There is no stopping rule as to the maximum treatment duration of avelumab plus axitinib in this indication. If either avelumab or axitinib has to be permanently discontinued on account of toxicity, treatment with the other drug can be continued as monotherapy as long as there is no evidence of progressive disease.

ANTI-EMETICS

Minimal emetic risk

CONCURRENT MEDICATION REQUIRED

Avelumab	Ensure premedication give before avelumab for first 4 cycles, then if the fourth infusion is completed without an infusion-related reaction, premedication for subsequent doses should be administered at the discretion of the physician.
Axitinib	Loperamide cycle 1

EXTRAVASATION AND TYPE OF LINE / FILTERS

Avelumab - neutral

Use 0.2micron low-protein binding in-line filter.
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥75
Thyroid function baseline, then every cycle
Random cortisol baseline, then every cycle
Random glucose every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Avelumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc
Axitinib	Diarrhoea Hand-foot syndrome Haemorrhage – increased risk of bleeding Hypertension Hypothyroidism Proteinurea Wound healing delayed

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

Axitinib	Anticoagulants

DOSE MODIFICATIONS
When dose reduction is necessary, the axitinib dose may be reduced to 3mg twice daily and further to 2mg twice daily.

Haematological
Axitinib
Temporarily interrupt axitinib if any bleeding event requires medical intervention.

Non-haematological
Avelumab
Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline

Axitinib

Hypertension	Blood pressure should be well-controlled prior to initiating axitinib. Patients should be monitored for hypertension and treated as needed with standard antihypertensive therapy. In the case of persistent hypertension, despite use of antihypertensive medicinal products, the axitinib dose should be reduced. For patients who develop severe hypertension, temporarily interrupt axitinib and restart at a lower dose once the patient is normotensive. If axitinib is interrupted, patients receiving antihypertensive medicinal products should be monitored for hypotension
Proteinuria	Moderate to severe proteinuria develops (≥2+ on dipstick, or >1g/24 hours), reduce dose or temporarily interrupt axitinib. Axitinib should be discontinued if the patient develops nephrotic syndrome.

Hepatic impairment

Avelumab

No dose adjustment is needed for patients with mild hepatic impairment. There are insufficient data in patients with moderate or severe hepatic impairment for dosing recommendations.

Axitinib

Child-Pugh scores are based on ascites, encephalopathy, INR, albumin, total bilirubin

Mild hepatic impairment (Child-Pugh A)	No dose adjustment
Moderate hepatic impairment (Child-Pugh B)	A dose decrease is recommended, the starting dose should be reduced from 5mg bd to 2mg bd
Severe hepatic impairment (Child-Pugh C).	Not recommended

Renal impairment

Avelumab

No dose adjustment is needed for patients with mild or moderate renal impairment. There are insufficient data in patients with severe renal impairment for dosing recommendations.

Axitinib

No dose adjustment is required in renal impairment.

REFERENCES

1. D'Angelo, S et al; JAMA Oncol 2018; 4(9):e180077. doi:10.1001/jamaoncol.2018.0077