Lancashire & South Cumbria Cancer Network
Systemic Anticancer Treatment Protocol

DRUG REGIMEN
Axitinib and avelumab

Indication for use
First line treatment of advanced renal cell carcinoma (RCC)

Regimen
Axitinib 5mg bd continuously (see dose modifications below)

Day	Drug	Fluid	Route	Time
1 & 15	Avelumab 800mg	250ml Sodium chloride 0.9%	IV	60 mins

Repeat every 4 weeks until disease progression or unacceptable toxicity

Give chlorphenamine IV 10mg and paracetamol 1000mg orally prior to the first 4 infusions

Investigation prior to initiating treatment
Investigations

- Blood pressure
- CT scan within last 4 weeks
- Baseline ECG
- FBC, U&E, LFT, Ca, glucose, TFTs
- Serum samples for HIV, hep C antibody and HBs Ag if risk factors
- Pregnancy test (if applicable)
- Height and Weight and vital signs

Gain informed consent
Give information sheet to patient

Cautions
Liver or renal failure
CYP3A4/5 inducing/inhibiting medications
Arterial/venous embolic or thrombotic events
Presence of HIV, hepatitis B or C
Patients on high dose immunosuppression
Autoimmune disease: history of active inflammatory bowel disease, history of symptomatic autoimmune disease e.g. rheumatoid arthritis, SLE, autoimmune vasculitis, history of autoimmune neuropathy e.g. Guillain-Barre
Patients should be on the lowest clinically effective dose of systemic steroids

Investigations and consultations prior to each cycle
FBC, U&Es, LFTs, Blood pressure

Acceptable levels for treatment to proceed (if outside these levels defer one week or contact consultant)
Proceed providing the following criteria are met:

- Hb > 9 g/dl
- WCC >2 $x10^9$/l
- Neut >1.0 $x10^9$/l
- Plts >100 $x10^9$/l
- Creatinine clearance >30mls/min
- AST < 3 x ULN
- Bilirubin <35
- Corrected QT interval <480 milliseconds
- BP <150/90 Acceptable levels for treatment to proceed

Assessment Visits

See on every 14 days for the first 28 days. Thereafter patient can be seen every 28 days. Patients may need to be seen more frequently if any particular toxicities are of concern.
At each visit check

- Toxicities
- Performance score
- Concomitant medications
- Blood pressure
- Weight
- FBC, U+E, LFT
- TFT every 12 weeks
- CT scan every 12 weeks

Side Effects axitinib

Stomatitis, taste changes, diarrhoea, nausea/vomiting, hypertension, hand/foot syndrome

Side effects avelumab

Infusion related reactions (pyrexia, chills, flushing, hypotension, dyspnoea, wheezing, back pain, abdominal pain, urticarial)

For grade 1 infusion related reactions, reduce infusion rate by 50%

For grade 2 infusion related reactions, withhold until adverse reactions recover to grade 0-1 and restart at a 50% slower rate.

For grade 3 infusion related reactions treatment should be permanently discontinued

Immune related adverse reactions (pneumonitis, hepatitis, colitis, endocrinopathies, renal dysfunction)

Consult the network immunotherapy toxicity guidelines for management of toxicities

Dose Modification Criteria axitinib

Elderly
There are no specific dosage recommendations based on the age of the patient.

Renal impairment
No dose reductions necessary for mild-moderate renal impairment where the estimated GFR is above 15ml/min. There is no data on more severe renal impairment and caution is advised.

Hepatic impairment
For mild hepatic impairment (Child-Pugh A), no dose adjustment is necessary.
For Child-Pugh B, start at 2mg bd
There is no data available on severe hepatic impairment and use is not recommended

Dose increases
If after two consecutive weeks at 5mg bd with tolerable toxicity no greater than grade 2 (unless the patient's blood pressure is > 150/90 mmHg or the patient is receiving antihypertensive treatment) the dose can be increased to 7mg bd. The dose can further be increased to a maximum of 10mg bd.

Dose reductions
Axitinib dose can be reduced to 3mg bd and then to no less than 2mg bd

Dose modification criteria avelumab

Dose modifications are not allowed: dose delays of up to 12 weeks are allowed.

Specific Information on Administration

If the patient vomits or misses a dose of axitinib, no additional doses should be taken. The next prescribed dose should be taken at the usual time

THIS PROTOCOL HAS BEEN DIRECTED BY DR PARIKH, DESIGNATED CLINICIAN FOR KIDNEY CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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