Regimen Reference Order

GENU - pembrolizumab (every 42 days) + aXitinib

ARIA: GENU – [pembrolizumab q 42 days + aXitinib]

Planned Course: **pembrolizumab every 42 days up to a maximum of 2 years (18 cycles) AND aXitinib twice daily until disease progression or unacceptable toxicity**

Indication for Use: **Advanced Renal Cell Carcinoma**

Drug Alert: **Immune Checkpoint Inhibitor (pembrolizumab)**

CVAD: **At Provider's Discretion**

Proceed with treatment if:

pembrolizumab + aXitinib

- ***ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 50 x 10^9/L***
- ***AST/ALT equal to or less than 3 times the upper limit of normal***
- ***Total bilirubin equal to or less than 1.5 times the upper limit of normal***
- ***Creatinine clearance equal to or greater than 30 mL/minute***

aXitinib Maintenance

- ***ANC equal to or greater than 0.5 x 10^9/L AND Platelets equal to or greater than 25 x 10^9/L***
- ***AST/ALT equal to or less than 3 times the upper limit of normal***
- ***Total bilirubin equal to or less than 1.5 times the upper limit of normal***
- ***Creatinine clearance equal to or greater than 30 mL/minute***

❖ **Contact Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements		
Drug	**Dose**	**CCMB Administration Guideline**
Not Applicable		

Treatment Regimen – GENU – pembrolizumab (every 42 days) + aXitinib		
Establish primary solution 500 mL of: normal saline		
Drug	**Dose**	**CCMB Administration Guideline**
pembrolizumab + aXitinib (Cycles 1 to 18)		
Day 1		
aXitinib	5 mg*	Orally twice daily with or without food Swallow whole **(Self-administered at home)**

pembrolizumab	4 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
Days 2 to 42		
aXitinib	5 mg*	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
aXitinib maintenance (Cycle 19 and Onwards)		
aXitinib	5 mg*	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
Maximum pembrolizumab dose is 400 mg All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See GENU DSG – Dose Banding document for more information		
***** At the discretion of the Medical Oncologist, aXitinib dose may be increased to 7 mg twice daily and subsequently to 10 mg twice daily if the patient is tolerating therapy OR dose may be reduced to 3 mg twice daily and subsequently to 2 mg twice daily if the patient is experiencing adverse drug reactions		
aXitinib (Inlyta®) available dosage strengths: 1 mg and 5 mg tablets **Classification: Cytotoxic, Hazardous**		

In the event of an infusion-related hypersensitivity reaction, refer to the '**Hypersensitivity Reaction Standing Order**'

REQUIRED MONITORING

- Blood pressure:
  - At baseline
  - After 1 week
  - Frequently thereafter (at least monthly)
- Urine protein:
  - Urinalysis for protein: Where urinalysis is not possible, use dipstick. If lab urinalysis for protein is greater than or equal to 1 g/L or dipstick proteinuria shows 2+ or 3+, notify prescriber
  - At baseline
  - Every 3 to 4 months or as clinically indicated

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin, glucose, TSH and blood pressure as per Physician Orders

pembrolizumab monitoring

- Medical oncologist or designate (i.e. family practitioner in oncology) must assess patient for immune-mediated adverse reactions prior to each cycle
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- No observation period is required after pembrolizumab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
None required		

DISCHARGE INSTRUCTIONS

All Cycles

- Patient should monitor blood pressure at home and record measurements on blood pressure log. This should be done daily for at least the first cycle
- Contact your cancer care team if systolic blood pressure is greater than or equal to 170 mmHg or diastolic blood pressure is greater than 95 mmHg on two consecutive readings
- aXitinib has potential for significant drug-drug interactions. Patients should notify clinic prior to starting any new medication
- Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade), and starfruit
- Reinforce applicable safe handling precautions of medications, blood and body fluids while on aXitinib

Cycles 1 to 18 (for pembrolizumab)

- Patient should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Confirm that patient has received the CCMB Immune Checkpoint Inhibitor Medical Alert wallet card
- Reinforce to patient the immune-mediated adverse reactions and importance of reporting immediately
    - For severe symptoms, the patient should be instructed to go to the nearest emergency room. Oncologist on call should be contacted

ADDITIONAL INFORMATION

- pembrolizumab is an Immune Checkpoint Inhibitor. Consult with oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- aXitinib can increase risk of hypertension, hemorrhage, wound healing complications and thromboembolic events
- aXitinib can cause rare but serious side effects such as GI perforation and fistulas, reversible posterior leukoencephalopathy syndrome (RPLS) and cardiac failure