Avelumab (Bavencio®)

Indication

Merkel cell carcinoma, metastatic

- CDF for first line
- NICE approved for second line

ECOG performance status 0-1
Women of childbearing potential and men with partners of childbearing potential, must be using adequate method of contraception throughout treatment and for 26 weeks after the last dose

Urothelial carcinoma
Monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) whose disease has not progressed with first-line platinum-based induction chemotherapy

Regimen details

Avelumab 800mg in 250ml 0.9% sodium chloride over 1 hour

Cycle frequency

Every 14 days

Number of cycles

Treat until disease progression or unacceptable toxicity. Maximum duration of treatment for urothelial cancer is 5 years.

Cautions

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

Administration

Administer the drug solution using a volumetric pump through an intravenous line containing a sterile non-pyrogenic, low protein binding in-line filter (pore size of 0.2 micrometer to 1.2micrometer)

Pre-medication

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

Emetogenicity

Minimally emetogenic

Additional supportive medication

None

Investigations – pre first cycle

FBC, U&Es, LFTs, Ca, glucose, TFTs, cortisol, LH, FSH, testosterone
Serum samples for HIV, hep C antibody and HBs Ag if risk factors
Pregnancy test (if applicable)
Height and Weight and vital signs

Investigations –pre subsequent cycles

Review in consultant clinic prior to first cycle and then at least on alternate cycles
ECOG performance status
FBC, U&Es, LFTs
TFTs
Glucose

Standard limits for administration to go ahead

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

WBC>2
ANC>1
Platelets>75
Hb>9
AST/ALT <2.5xULN if no liver mets, <5xULN if liver mets
Bilirubin<1.5xULN
Creatine clearance > 30ml/min

Check with consultant prior to any deferrals

Dose modifications

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

Adverse effects –

for full details consult product literature/ reference texts

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)
Reported grade 3 or 4 side effects include lymphopenia, raised LFTs, infusion reactions, synovitis, nephritis, colitis; other common toxicities were anaemia, hypothyroidism, decreased appetite, headache, dizziness, peripheral neuropathy, N&V, diarrhoea, constipation, abdominal pain, rash, fatigue, pyrexia, peripheral oedema. However, the following toxicities are common to all PDL1/PD1 inhibitors:

Immune-Mediated Pneumonitis
Monitor patients for signs and symptoms of pneumonitis. Administer corticosteroids for grade 2 or greater pneumonitis. Permanently discontinue avelumab for grade 3 or 4 and withhold avelumab until resolution for grade 2.

Immune-Mediated Colitis
Monitor patients for immune mediated colitis. Administer corticosteroids for grade 2 (of more than 5 days duration), 3 or 4 colitis. Withhold avelumab for grade 2 or 3 until resolution. Permanently discontinue avelumab for grade 4 colitis or recurrent colitis upon restarting avelumab.

Immune-Mediated Hepatitis
Monitor patients for abnormal LFTs prior to and during treatment. Administer corticosteroids for grade 2 or greater transaminase elevations. Withhold avelumab for grade 2 until resolution and permanently discontinue avelumab for grade 3 or 4 immune-mediated hepatitis.

Immune-Mediated Nephritis and Renal Dysfunction
Monitor patients for elevated serum creatinine prior to and during treatment. For grade 2 or 3 serum creatinine

elevation, withhold avelumab and administer corticosteroids, if worsening or no improvement occurs permanently discontinue avelumab. For grade 4 administer corticosteroids and permanently discontinue avelumab.

Immune-Mediated Hypothyroidism and Hyperthyroidism
Monitor TFTs prior to treatment. Administer thyroid replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism.

Immune-Mediated Rash
Severe rash has been observed with immunotherapies, which may be immune-related. For grade 3 rash, withhold avelumab and administer corticosteroids, if worsening or no improvement occurs, permanently discontinue avelumab. For grade 4 administer corticosteroids and permanently discontinue avelumab.

Other less common Immune-Mediated Adverse reactions
- Adrenal insufficiency
- Pituitary insufficiency
- Diabetes
- Pancreatitis
- Uveitis
- Neuropathy
- Vasculitis

Based on the severity of the adverse reaction, administer high dose corticosteroids and if appropriate, initiate hormone replacement therapy.

References

Avelumab SPC - https://www.medicines.org.uk/emc/product/8453 - accessed 12/04/2022

Avelumab for treating metastatic Merkel cell carcinoma Technology appraisal guidance [TA517] Published date: 11 April 2018

Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy – NICE guidance in development [ID3735]

Kaufman HL, Russell J, Hamid O, et al. Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicentre, single-group, open-label, phase 2 trial. Lancet Oncol. 2016;17(10):1374-1385.

THIS PROTOCOL HAS BEEN DIRECTED BY DR PARIKH, CONSULTANT CLINICAL ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: July 2022
Review: July 2024
VERSION: 5