Systemic Anti Cancer Therapy Protocol

Cemiplimab
Cutaneous Squamous Cell Carcinoma

Protocol Reference: MPHACEMSK
(Version No: 1.0)

Approved for use in:

- Frist line treatment of histologically or cytologically confirmed locally advanced or metastatic cutaneous squamous cell carcinoma, which is not a candidate for curative surgery or curative radiotherapy.
- ECOG performance status score must be 0 or 1.
- Patient must have no symptomatically active brain or leptomeningeal metastases.
- Blueteq registration is required.

Dosage:

Drug	Dose	Route	Frequency
Cemiplimab	**350mg**	**IV infusion**	**Day 1 only of a 21 day cycle**

Maximum treatment duration of 2 years (or 35 3-weekly cycles of cemiplimab) – whichever occurs first.

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Cemiplimab	350mg	IV infusion	100mL sodium chloride 0.9%. Infused over 30 minutes in a non-pyrogenic line with a 0.2 micron filter

Routine prophylaxis against infusion related reactions is not required.

However the patient should be monitored during the infusion, and treatment given if necessary (antihistamines, steroids etc).

Extravasation risk:

Monoclonal antibody – treat symptomatically, no specific recommendations.

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal	Cemiplimab	No dose adjustment is recommended, however there is limited data for patients with severe renal impairment (CrCl <30ml/min).

Hepatic	Cemiplimab	No dose adjustment is recommended for patients with mild hepatic impairment; however cemiplimab has not been studied in patients with moderate or severe hepatic impairment.

Interactions:

No pharmacokinetic drug-drug interaction studies have been conducted with cemiplimab. The use of systemic corticosteroids or immunosuppressants before starting cemiplimab, except for physiological doses of systemic corticosteroid (≤10 mg/day prednisone or equivalent), should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of cemiplimab. However, systemic corticosteroids or other immunosuppressants can be used after starting cemiplimab to treat IRARs.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Cemiplimab**	**350mg**	**IV**	Sodium Chloride 0.9% 100mL over 30 minutes

Main toxicities:

Cemiplimab	
Immune-Mediated Pneumonitis	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Immune-Mediated Colitis	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Other Immune-Mediated Toxicities: Hypophysitis Nephritis Hyperthyroidism or Hypothyroidism Less frequently: Exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, haemolytic anaemia	Monitor LFTs, biochemistry, cortisol and TFTs regularly Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Other non-immune adverse events: Fatigue, anaemia Cough, dyspnoea Nausea, decreased appetite Pruritis, rash Constipation, diarrhoea Arthralgia	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Laboratory abnormalities: Hyponatraemia, hypocalcaemia, hyperglycaemia, hypertriglyceridaemia	Refer to Immuno-Oncology toxicity specific guidance for adverse event management

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Prior to cycle 3	Cycle 3	Ongoing
Informed Consent	X					
Clinical Assessment	X			X		Every 12 weeks thereafter or as clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X		X	Every cycle
FBC, U&E, Magnesium, LFTs, LDH	X	X	X		X	Every cycle
TFTs, cortisol, blood glucose, lipid profile (cholesterol).	X				X	Every 6 weeks/if clinically indicated
CrCl (Cockcroft and Gault)	X					Every cycle only if baseline CrCL <40ml/min or creatinine increases above 1.5x upper limit of normal
CT scan	X					Every 12 weeks/if clinically indicated
ECG						If clinically indicated
Blood pressure measurement	X	X	X		X	Every cycle
Respiratory Rate						If clinically indicated
Weight recorded	X	X	X		X	Every cycle

Pregnancy test if applicable
Serum samples for HIV, Hep C antibody and HBsAg if risk factors

Dose Modifications and Toxicity Management:

Proceed on day 1 of cycle if:-

Hb > 9g/L	ANC ≥ 1.0 x 10^9/L	Platelets ≥ 75 x 10^9/L

Confirm any deferrals with the prescribing oncologist.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

Toxicity Grade	Action
Grade 1	No action. Provide symptomatic treatment
Grade 2	Withhold until resolved to <grade 1. Refer to Immuno-Oncology toxicity specific guidance for adverse event management.
Grade 3 and Grade 4	Discontinue. Refer to Immuno-Oncology toxicity specific guidance for adverse event management Discontinue if unable to reduce corticosteroid dose to < 10 mg per day prednisolone equivalent within 12 weeks of toxicity.

Cemiplimab will be permanently discontinued for any Grade 3-4, severe or life-threatening adverse reaction.

Hepatic impairment	
AST or ALT increase to 3 to 5 times the upper limit of normal (ULN) Bilirubin increase to 1.5 to 3 times ULN	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
AST or ALT increase to greater than 5 times ULN Bilirubin increase to greater than 3 times ULN	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
In patient with liver metastasis with baseline AST or ALT at 3 to 5 times the ULN And increase by > 50% and lasting for more than one week	Refer to Immuno-Oncology toxicity specific guidance for adverse event management

Renal Impairment

No studies have been conducted on patients with severe renal impairment.
No dose adjustments are required for mild to moderate renal impairment.

References:

1. https://www.medicines.org.uk/emc/product/10438
2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)
3. Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)