Systemic Anti Cancer Treatment Protocol

Pembrolizumab Malignant Melanoma

PROTOCOL REF: MPHAMMEPEM (Version No: 1.2)

Pembrolizumab is a humanised monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2.

The PD-1 pathway represents a major immune control switch which may be engaged by tumour cells to overcome active T-cell immune surveillance.

Approved for use in:

- **Advanced (unresectable or metastatic) melanoma.**
- **Adjuvant treatment of newly diagnosed & completely resected stage 3 melanoma for a maximum of 12 months.**

***** Blueteq registration is required in the adjuvant setting *****

Exclusions

History of pneumonitis, organ transplantation, autoimmune disorders, HIV infection, active hepatitis B or C infection

Active infection requiring systemic treatment

Less than 4 weeks from major surgery

History of clinically severe autoimmune disease

Dosage:

Drug	Dosage	Route	Frequency
Pembrolizumab	200mg	IV infusion	3 weekly

Metastatic: Repeated every 3 weeks until disease progression or unacceptable toxicity.

Adjuvant: Repeated every 3 weeks until disease progression or unacceptable toxicity for a maximum of 12 months.

Extravasation risk:

Monoclonal antibody – treat symptomatically, no specific recommendations.

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Pembrolizumab	200mg	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.)

Main Toxicities:

Immune-Mediated Pneumonitis Pneumonitis occurred in 3% of melanoma patients (including G3 in 0.2%).	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Immune-Mediated Colitis Colitis occurred in 1% of patients (including G3 in 0.5%).	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	C1	C2		C3		C4		C5	Ongoing
		Week 1	Week 4		Week 7	Week 9	Week 10		Week 13	
Oncology Team Assessment	X					X*			X	Every 12 weeks thereafter or as clinically indicated
Informed Consent	X									
Nursing Assessment Including toxicity assessment *Home treatments- 24-48 hours before due dose*		X	X		X		X		X	Every cycle
FBC, U&E, LFTs and LDH *Local hospital/GP surgery 72 hours before due dose*	X		X		X		X		X	Every Cycle
TFTs and cortisol *Local hospital/GP surgery 48 hours before due dose*	X		X		X		X		X	Every Cycle
Blood glucose	X		X		X		X		X	Every Cycle
Lipid profile (cholesterol)										Only if clinically indicated
CT scan**	X									Every 12 weeks or as clinically indicated
Blood pressure & full set of observations	X	X	X		X		X		X	Every cycle
ECOG PS	X	X	X		X		X		X	Every cycle
Weight recorded	X	X	X		X		X		X	Every cycle

Home treatment if eligible

Imaging with review by oncology team 1 week later

*Formal medical review (can be virtual) to assess the tolerability of treatment and whether treatment should continue (as per NHS England criteria to occur before the end of first 9 weeks treatment).

**CT Scan only required every 6 months in adjuvant setting.

Pregnancy test if applicable.

Serum samples for HIV, Hep C antibody and HBsAg if risk factors.

Dose Modifications and Toxicity Management:

Haematological toxicity

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.

Non-haematological toxicity

Toxicity Grade	Action
Grade 1	No action. Provide symptomatic treatment
Grade 2	Withhold Pembrolizumab until resolved to <grade 1. Refer to Immuno-Oncology toxicity specific guidance for adverse event management.
Grade 3 and Grade 4	Discontinue Pembrolizumab. 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.

Pembrolizumab 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.

Patient Counselling Points

Contact the triage team for the following:

New or worsening cough, chest pain or shortness of breath

Diarrhoea or severe abdominal pain

Jaundice, severe nausea or vomiting, or easy bruising or bleeding

Persistent or unusual headache, extreme weakness, dizziness or fainting, or vision changes

Monitor for signs of infection / sepsis

References:

SmPC from USA Sept 2014 MSD

NICE TA 357 and TA366

KEYNOTE-002

Lancet Oncol 2015 16: 908-918

Ribas A et al