PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

PEMBROLIZUMAB
Relapsed/Refractory (R/R) Hodgkin's Lymphoma

PROTOCOL REF: MPHAPHLHA
(Version No. 2.0)

Approved for use in:

- R/R Hodgkin's Lymphoma in patients who have previously had a stem cell transplant but have not received brentuximab nor any prior treatment with any antibody which targets PD-1 or PD-L1 or PD-L2 or CD137 or OX40 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4)
- R/R Hodgkin's Lymphoma in patients who have had 2 previous lines of treatment but have **not** previously had a stem cell transplant nor brentuximab nor any prior treatment with any antibody which targets PD-1 or PD-L1 or PD-L2 or CD137 or OX40 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4)

A Blueteq application is required

Dosage:

Drug	Dose	Route	Frequency
Pembrolizumab	**200mg**	IV infusion	Day 1 only of a 21 day cycle
OR			
Pembrolizumab	**400mg**	IV infusion	Day 1 only of a 42 day cycle

Treatment will be stopped after 2 years of treatment or on disease progression, unacceptable toxicity or stem cell transplantation.

Administration:

- Treatment breaks of up to 12 weeks from expected cycle date are allowed but a Blueteq treatment form must be completed if the treatment break is any longer.
- Atypical responses (i.e. an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until disease progression is confirmed
- A patient alert card must be given to the patient with each prescription
- Women of childbearing potential should use effective contraception during treatment with pembrolizumab and for at least 4 months after the last dose of pembrolizumab
- Contact the triage team for the following:
    - New or worsening cough, chest pain or shortness of breath
    - Diarrhoea or severe abdominal pain (with or without blood/mucous)
    - 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

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

No supportive medicines routinely given with pembrolizumab.

Extravasation risk:

Non-vesicant

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

Interactions:

No formal pharmacokinetic drug interaction studies have been conducted with pembrolizumab. Since pembrolizumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Pembrolizumab**	**200mg or 400mg**	**IV**	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.)

Please refer to the CCC Hypersensitivity; Management Prevention Policy

Main toxicities:

Non-immune adverse effects: fatigue, thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, infections and infusion related reactions.

For full details on assessment and management of immune-related toxicities refer to CCC immune-Oncology toxicity specific guidance for adverse effect management at below link.

https://www.clatterbridgecc.nhs.uk/professionals/guidance/immunotherapy

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

Allogeneic HSCT after treatment with pembrolizumab

Cases of graft-versus-host-disease (GVHD) and hepatic veno-occlusive disease (VOD) have been observed in patients with Hodgkin's lymphoma undergoing allogeneic HSCT after previous exposure to pembrolizumab. Until further data become available, careful consideration to the potential benefits of HSCT and the possible increased risk of transplant-related complications should be made case by case.

Allogeneic HSCT prior to treatment with pembrolizumab

In patients with a history of allogeneic HSCT, acute GVHD, including fatal GVHD, has been reported after treatment with pembrolizumab. Patients who experienced GVHD after their transplant procedure may be at an increased risk for GVHD after treatment with pembrolizumab. Consider the benefit of treatment with pembrolizumab versus the risk of possible GVHD in patients with a history of allogeneic HSCT.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment	X	X	X	X	As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)	X	X	X	X	Every cycle
Immunotherapy bloods as per Meditech order set: FBC, U&E/renal profile, Magnesium, LFTs (AST, ALT and bilirubin), TFTs, cortisol, blood glucose, LDH, CRP	X	X	X	X	Every cycle
CrCl (Cockcroft and Gault)	X	X	X	X	Every cycle
PET CT scan	X				At the end of treatment and if clinically indicated
TFTs, cortisol, blood glucose, HbA1c	X	X	X	X	Every cycle
Lipid profile	X				At baseline then if clinically indicated
Fatigue profile as per Meditech order set: B12, folate, Iron profile, vitamin D, Zinc, Testosterone (men only), ESR	X				At baseline then if clinically indicated
Trop-T, CK, pro-BNP	X				At baseline then if clinically indicated
ECG	X				At baseline then if clinically indicated
Full set of observations (*BP, heart rate, temperature, respiratory rate and O_2 sats*)	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 0.5 x 10^9/L	Platelets ≥ 25 x 10^9/L

Restart when ANC have recovered to >1.5 x 10^9/L and platelets have recovered to >75 x 10^9/L. No dose reductions are recommended.

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:

Dosing in renal and hepatic impairment:

Renal	No dose adjustment is needed for patients with mild or moderate renal impairment (CrCl >30ml/min). Pembrolizumab has not been studied in patients with severe renal impairment. If a deterioration of renal function is seen then immune related nephritis should be considered.

Hepatic	No dose adjustment is needed for patients with mild or moderate hepatic impairment. Pembrolizumab has not been studied in patients with severe hepatic impairment. If a deterioration of hepatic function is seen then immune related hepatitis should be considered

References:

1. https://www.medicines.org.uk/emc pembrolizumab. Accessed 14/3/23. Date of revision 16/11/22.
2. Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 2 previous therapies. Technology appraisal guidance [TA772] Published: 23 February 2022.

3. Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma. Technology appraisal guidance [TA540] Published: 03 September 2018

Circulation/Dissemination

Date added into Q-Pulse	17th August 2023
Date document posted on the Intranet	N/A

Version History

		Author name and designation	Summary of main changes
		Kelly Crampton	New protocol
May 2023	2.0	Aileen McCaughey (Haematology Pharmacist)	Blueteq criteria updated, new template used. 400mg dose included. IO toxicity detail added.