PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Nivolumab
Relapsed/Refractory Hodgkin's Lymphoma

PROTOCOL REF: MPHANHLHA
(Version No. 2.0)

Approved for use in:

- Patients with R/R Hodgkin's Lymphoma who have previously had an autologous stem cell transplant and been treated with brentuximab.
- Patients must have no known CNS lymphoma and has not received treatment with an anti-PD-1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.

Blueteq registration required

Dosage:

Drug	Dose	Route	Frequency
Nivolumab	240mg	IV	Every 2 weeks
OR			
Nivolumab	480mg	IV	Every 4 weeks

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

Administration:

- 480mg every 4 weeks is an off-label use of nivolumab that is allowed in the Blueteq criteria

- 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 5 months after the last dose of nivolumab
- Dose escalations or reductions are not recommended
- 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 with nivolumab for clinically stable patients with initial evidence of disease progression until disease progression is confirmed.
- 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 nivolumab

Extravasation risk:

Non-vesicant

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

Interactions:

No interactions are expected with nivolumab

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Nivolumab**	**240mg**	**IV**	In 100mls sodium chloride 0.9% over 30 minutes via a 0.2micron filter
OR				
1	**Nivolumab**	**480mg**	**IV**	In 100mls sodium chloride 0.9% over 60 minutes via 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 nivolumab

Cases of graft-versus-host-disease (GVHD) and transplant related mortality have been observed in patients with Hodgkin's lymphoma undergoing allogeneic HSCT after previous exposure to nivolumab. 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 nivolumab

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 nivolumab. Consider the benefit of treatment with nivolumab versus the risk of possible GVHD in patients with a history of allogeneic HSCT and GVHD.

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 ≥ 1.0 x 10^9/L	Platelets ≥ 75 x 10^9/L

In the case of cytopenias contact the clinician to consider a break in treatment.

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). Nivolumab 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	Nivolumab should be used with caution in patients with moderate or severe hepatic impairment (i.e. a raised ALT and a bilirubin > 32 micromols/L). If LFTs deteriorate during treatment then immune related hepatitis should be considered.

References:

1. https://www.medicines.org.uk/emc nivolumab. Accessed 24/03/2023. Last updated 02/11/2022
2. NICE TA462. Nivolumab for treating relapsed or refractory classical Hodgkin's Lymphoma. The National Institute for Health and Care Excellence (2017).

Circulation/Dissemination

Date added into Q-Pulse	10th August 2023
Date document posted on the Intranet	

Version History

		Author name and designation	Summary of main changes
		Kelly Crampton	New protocol
May 2023	2.0	**Aileen McCaughey (Haematology Pharmacist)**	Updated to current SACT protocol template, 480mg dose and link to IO toxicity protocols included.