PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Brentuximab Vedotin

Hodgkin's Lymphoma, Systemic Anaplastic Large Cell Lymphoma and CD30+ Cutaneous T-cell Lymphoma

PROTOCOL REF: MPHABREHA
Version 2.0

Approved for use in:

- Treatment of brentuximab-naïve relapsed/refractory CD30+ Hodgkin lymphoma following at least 2 prior therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option in adult patients. **NICE TA524**
- Treatment of brentuximab-naïve relapsed/refractory CD30+ Hodgkin lymphoma following autologous stem cell transplant in adult patients. **NICE TA524**
- Re-use of brentuximab in relapsed/refractory CD30+ Hodgkin lymphoma after autologous stem cell transplantation in patients who have previously achieved a partial/complete response to brentuximab, and brentuximab is being used as a bridge to allogenic stem cell transplant or donor lymphocyte infusion (DLI).
- The treatment of relapsed or refractory systemic anaplastic large cell lymphoma in adult patients. **NICE TA478**
- The treatment of CD30+ cutaneous T cell lymphoma following at least 1 prior systemic therapy only if the patient has mycosis fungoides stage IIB or greater, primary cutaneous anaplastic large cell lymphoma or Sezary syndrome.**. NICE TA577**

Blueteq application is required for all indications

Dosage:

Drug	Dose	Route	Frequency
Brentuximab vedotin	1.8mg/kg (max dose 180mg)	IV	Day 1

Maximum of 16 cycles (every 21 days). Discontinue after 4 cycles if CT/PET-CT shows less than partial or complete response.

Administration (+/- Counselling Points):

- Patients should be closely monitored for new or worsening neurological, cognitive, or behavioural signs or symptoms, which may be suggestive of progressive multifocal leukoencephalopathy (PML).
- Immediate and delayed infusion-related reactions (IRR), as well as anaphylactic reactions, have been reported. Routine use of pre-medications is not required, however patients should be carefully monitored during and after infusion. If an anaphylactic reaction occurs, brentuximab vedotin should be immediately and permanently discontinued and appropriate medical therapy should be administered.
- If an infusion related reaction (IRR) occurs, the infusion should be interrupted and appropriate medical management instituted. The infusion may be restarted at a slower rate after symptom resolution. Patients who have experienced a prior IRR should be pre-medicated for subsequent infusions. Premedication may include paracetamol, an antihistamine and a corticosteroid.

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

- Allopurinol 300mg or 100mg (dose dependant on renal function) OD for the first cycle
- Co-trimoxazole 480mg OD

Extravasation risk:

Brentuximab - non-vesicant

Dosing in renal and hepatic impairment:

Renal	
CrCl (ml/min)	**Dose adjustment**
<30 or haemodialysis	1.2mg/kg
Hepatic	
Child-Pugh Score	**Dose adjustment**
A	1.2mg/kg
B or C	Not recommended

Interactions:

Co-administration of brentuximab with:

- Strong CYP3A4 and P-gp inhibitors (e.g. ketoconazole) may increase the incidence of neutropenia.
- Rifampicin (a strong CYP3A4 inducer) appeared to reduce plasma concentrations of MMAE (the active component of brentuximab). If the combination is required then close monitoring is required to ensure the brentuximab remains effective.
- Co-administration of brentuximab and bleomycin is contraindicated due to unacceptable pulmonary toxicity

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Brentuximab**	**1.8mg/kg (max dose 180mg)** **If the patient's weight is more than 100 kg, the dose calculation should use 100 kg**	**IV**	Over 30 minutes in 100-250ml sodium chloride 0.9% **(Final concentration should be between 0.4 - 1.2 mg/ml.)**

Main toxicities:

Brentuximab
Thrombocytopenia, neutropenia, anaemia, fatigue, nausea, vomiting, diarrhoea, constipation, arthralgia, cough, dyspnoea, rash, pruritis, progressive multifocal leukoencephalopathy (PML), infections, herpes zoster/simplex, oral candidiasis, hyperglycaemia, peripheral neuropathy, dizziness, alopecia, hepatotoxicity, AST/ALT increase. Uncommon: pancreatitis, Steven Johnson Syndrome, DRESS, anaphylaxis

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Informed consent	X					
Clinical Assessment		X	X	X	X	As clinically indicated or at the end of treatment
SACT Assessment (including performance status and toxicity assessment)		X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFTs & Calcium profile	X	X	X	X	X	Every Cycle
Serum amylase and lipase						If clinically indicated
CrCl (Cockcroft and Gault)	X					Repeat as clinically indicated
PET CT scan (not required for patients with Cutaneous T-Cell Lymphoma)	X				X	Repeat every 4 cycles
Height	X					
Weight recorded	X	X	X	X	X	Every cycle
Pregnancy test	X					If clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed if-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

If counts are below these values then withhold brentuximab until counts have recovered and then resume at the same dose and schedule, but consider GCSF for future cycles. Patients who develop Grade 3 or Grade 4 lymphopenia may continue treatment without interruption.

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.

Neuropathy:

Dosing recommendations for new or worsening peripheral sensory or motor neuropathy

Severity of peripheral sensory or motor neuropathy*	Modification of dose and schedule
Grade 1 (paraesthesia and/or loss of reflexes, with no loss of function)	Continue with the same dose and schedule
Grade 2 (interfering with function but not with activities of daily living) or	Withhold dose until toxicity returns to ≤ Grade 1 or baseline, then restart treatment at a reduced dose of 1.2 mg/kg up to a maximum of 120 mg every 3 weeks
Grade 3 (interfering with activities of daily living)	Withhold dose until toxicity returns to ≤ Grade 1 or baseline, then restart treatment at a reduced dose of 1.2 mg/kg every 3 weeks up to a maximum of 120 mg every 3 weeks
Grade 4 (sensory neuropathy which is disabling or motor neuropathy that is life threatening or leads to paralysis)	Discontinue treatment

* Grading based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v3.0; see neuropathy: motor; neuropathy: sensory; and neuropathic pain.

References:

1. NICE: TA524: Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma. Published 13th June 2018. Accessed 14/07/23
2. NICE: TA478: Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell lymphoma. Published 4th October 2017. Accessed 14/07/23
3. NICE: TA577: Brentuximab vedotin for treating CD30-positive cutaneous T-cell lymphoma. Published 24th April 2019. Accessed 14/07/23
4. Adcetris - Brentuximab vedotin. Takeda UK Ltd. Last updated 16th June 2022. Avaialable: Adcetris 50 mg powder for concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) . Last accessed: 04/07/23
5. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.

Circulation/Dissemination

Date added into Q-Pulse	For completion by DCM
Date document posted on the Intranet	For completion by DCM

Version History

		Author name and designation	Summary of main changes
May 2020	1.0	**Aileen McCaughey**	**Protocol created**
July 2023	2.0	**Jade Marsh**	**Protocol review. Indications updated. Transferred to new template. IRR information added.**