(R) Mini BEAM

Indication
Relapsed/Refractory Hodgkin and non-Hodgkin lymphoma

ICD-10 codes
Codes with prefix C81-C86

Regimen details

Day	Drug	Dose	Route
1	Rituximab*	375mg/m^2 daily	IV infusion
1	Carmustine	60mg/m^2 daily	IV infusion
2-5	Cytarabine	100mg/m^2 **twice daily**	IV infusion
2-5	Etoposide	75mg/m^2 daily	IV infusion
6	Melphalan‡	30mg/m^2 daily	IV infusion

*if appropriate
‡Hydration required for melphalan, (see below)

Consider GCSF as primary prophylaxis from D7 for 7 days or as per local guidelines.

Cycle frequency
Repeated every 21-28 days, depending on sufficient blood count recovery (i.e neutrophils >1.0 x 10^9/L and platelets (unsupported) > 100x 10^9/L

Number of cycles
Up to a maximum of 3 courses

Administration
Rituximab is administered in 500ml sodium chloride 0.9%. The first infusion should be initiated at 50mg/hour and if tolerated the rate can be increased at 50mg/hour every 30 minutes to a maximum of 400mg/hour.
Subsequent infusions should be initiated at 100mg/hour and if tolerated increased at 100mg/hour increments every 30 minutes to a maximum of 400mg/hour.

Carmustine is administered in 500ml sodium chloride 0.9% over 1 hour.

Cytarabine is administered in 100ml sodium chloride 0.9% over 30 minutes at 12 hourly intervals.

Etoposide is administered in 500-1000ml sodium chloride 0.9% (concentration dependent) over 2 hours.

Melphalan Pre-hydration
Sodium chloride 0.9% 1000ml over 30 minutes
Furosemide 20mg IV bolus
Ensure urine output is ≥ 500ml/hour (if insufficient repeat furosemide dose)

Melphalan is administered in 500ml sodium chloride 0.9% over 30 minutes

Melphalan post-hydration
Sodium chloride 0.9% 1000ml over 30 minutes
DO NOT allow the patient to get into significantly positive fluid balance- give furosemide as appropriate

Pre-medication

Pre-hydration and furosemide pre melphalan as above
Anti-emetics as per local policy

Emetogenicity

Day 1 has high emetogenic potential
Day 2-5 has low emetogenic potential
Day 6 has moderate emetogenic potential

Additional supportive medication

Allopurinol 300mg OD (100mg OD if CrCl <20ml/min) for the first 2 weeks
Anti-emetics as per local policy
Antiviral, antifungal and PCP prophylaxis as per local policy
Prophylactic antibiotics may be required e.g. ciprofloxacin (or as per local policy) when neutrophil count <0.5 x 10^9/L
Mouthwashes as per local policy
H_2 antagonist or proton-pump inhibitor if required
Consider starting GCSF on D7 for 7 days as per local policy

Extravasation

Carmustine is a vesicant (Group 5)
Cytarabine and Melphalan are neutral (Group 1)
Etoposide is an irritant (Group 3)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&Es (including creatinine)	14 days
LFTs	14 days
LDH	14 days
Calcium	14 days
Magnesium	14 days

Other pre-treatment investigations:
Hepatitis B (surface antigen and core antibody status)
Hepatitis C antibody
HIV 1 and 2 antibody screen

Investigations – pre subsequent cycles

Investigation	Validity period
FBCs	72 hours
U&Es (including creatinine)	72 hours
LFTs	72 hours
Magnesium	72 hours
Calcium	72 hours

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥1.0 x 10^9/L*
Platelets	≥100 x 10^9/L*
Creatinine Clearance	≥60ml/min
Bilirubin	≤1.25 x ULN
ALT	≤1.0 x ULN

*Unless cytopenias are disease related

Dose modifications

- **Haematological toxicity**

If neutrophil count is <1.0 x 10^9/L or platelets <100 x 10^9/L, delay by one week and recheck full blood count before proceeding

- **Renal impairment**

CrCl (ml/min)	Carmustine dose
≥60	100%
45-60	80%
30-45	75%
<30	Clinical decision

CrCl (ml/min)	Etoposide dose
≥50	100%
15-50	75%
<15	50%

GFR (ml/min)	Melphalan dose
≥50	100%
30-50	50%
<30	Clinical decision

Cytarabine - No dose reduction necessary in this protocol.

- **Hepatic impairment**

Carmustine - No dose adjustment is recommended, clinical decision.

Melphalan – No dose adjustment is recommended, clinical decision.

Cytarabine doses should be reduced to 50% if bilirubin > 1.5 x ULN. Doses may be escalated in subsequent cycles in the absence of toxicity (consultant decision).

Etoposide – if bilirubin <2.5 x ULN with normal albumin and renal function, no dose reduction indicated. If bilirubin >2.5 x ULN **or** decreased albumin levels, consider dose reduction to 50% dose and increase if tolerated.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Severe nausea and vomiting
Pulmonary fibrosis
Hypotension
Nephrotoxicity
Hepatoxicity
Peripheral neuropathy
Hyperbilirubinemia
Hepatic dysfunction
Allergic reactions (including anaphylaxis)

- **Frequently occurring side effects**

Myelosuppression
Pulmonary toxicity
Rash
Fever
Facial flushing
Mucositis
Diarrhoea

- **Other side effects**

Cytarabine syndrome (fever, myalgia, rash)
Intense venous pain if carmustine infused rapidly peripherally
Gynaecomastia
Oral/anal inflammation/ulceration
Alopecia

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Switch patient to a low molecular weight heparin during treatment

Etoposide
Ciclosporin: High dose ciclosporin markedly increases etoposide levels
Enzyme inducing antiepileptics: metabolism of etoposide may be increased by phenytoin, phenobarbital and possibly carmustine
Phenylbutazone, sodium salicylate and salicylic acid: can affect protein binding of etoposide

Cytarabine
Clozapine: increased risk of agranulocytosis- avoid concomitant use
Digoxin: cytarabine may affect plasma digoxin levels – consider monitoring

Melphalan
Nephrotoxic drugs: increased risk of nephrotoxicity when melphalan given in combination with nephrotoxic drugs

Carmustine
Phenytoin: reduced activity of antiepileptic medicines when used concomitantly
Cimetidine: concomitant use leads to delayed, major, suspected, increased toxic effects of carmustine due to in the inhibition of carmustine metabolism
Digoxin: suspected decreased effects of digoxin due to decreased digoxin absorption

Additional Information

Nil

References

- Ashley C., Dunleavy A. The renal drug handbook: the ultimate prescribing guide for renal practitioners. 5th ed. London: CRC Press; 2018.
- Aspen. Melphalan 50mg Powder and Solvent for Solution for Injection/Infusion [internet] 2014. [cited 2020 July 29] Available via www.medicines.org.uk
- 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.
- Medac GmbH. Etoposide 20mg/ml Concentrate for solution for infusion [internet] 2019.[Cited 2020 July 29] Available via www.medicines.org.uk
- Moore, S., Kayani, I., Peggs, K., et al. Mini-BEAM is effective as a bridge to transplantation in patients with refractory or relapsed Hodgkin lymphoma who have failed to respond to previous lines of salvage chemotherapy but not in patients with salvage-refractory DLBCL. *British Journal of Haematology* 2012; 157, 543-552
- Girouard, C., Dufresne, J. et al Salvage chemotherapy with mini-BEAM for relapsed or refractory non-Hodgkin's lymphoma prior to autologous bone marrow transplantation. *Annals of Oncology* 1997; 8:657-680
- Tilomed Laboratories Ltd. Carmustine 200mg Powder and solvent for Solution for Infusion [internet] 2020. [cited 2020 July 29] Available via www.medicines.org.uk
- The North London Cancer Network. Dosage adjustment for cytotoxics in hepatic impairment. 3rd ed. London: University College London Hospitals Foundation Trust, 2009.
- The North London Cancer Network. Dosage adjustment for cytotoxics in renal impairment. 3rd ed. London: University College London Hospitals Foundation Trust, 2009.

Written/reviewed by: Jessica O'Neill (Senior Haematology and BMT Pharmacist, UHBW NHS Trust), Dr Nikesh Chavda (Consultant Haematologist, UHBW NHS Trust)

Checked by: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance)

Authorised by: Dr Jeremy Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

Date: June 2021