BEAM high dose therapy with autologous stem cell support (Lymphoma)

Indication

High dose chemotherapy with autologous stem cell support for patients with relapsed/refractory Hodgkin and non-Hodgkin lymphoma

Consider in first line setting as consolidation for patients with T-cell lymphoma

Patients must have had an adequate peripheral blood stem cell collection and be under the care of the stem cell transplant team

ICD-10 codes

Codes with prefix C81-85

Regimen details

Day	Drug	Dose	Route	Comments
-7	Carmustine*	300mg/m^2 once daily	IV infusion	Give on time due to short expiry
-6 to -3	Etoposide	200mg/m^2 once daily	IV infusion	
-6 to -3	Cytarabine	200mg/m^2 twice daily	IV infusion	Doses should be 12 hours apart
-2	Melphalan**	140mg/m^2 once daily	IV infusion	Give on time due to short expiry
0	**Stem cell infusion**			

* If carmustine is unavailable then substitution with lomustine 200mg/m^2 PO once daily on day -7 can be considered – consultant decision

**Pre- and post-hydration is required for melphalan, see below.

Cycle frequency

N/A

Number of cycles

N/A

Administration

Scheduling should take into account the short expiry of both carmustine and melphalan. Discuss with specialist pharmacist.

Carmustine is administered in 500mL sodium chloride 0.9% and infused over 2 hours.

Etoposide is administered in 1000mL sodium chloride 0.9% and infused over 4 hours

Cytarabine is administered in 100mL sodium chloride 0.9% and infused over 30 minutes

Melphalan must be given on time due to its short expiry. Melphalan is administered in 500mL sodium chloride 0.9% and infused over 30 minutes. Pre- and post-hydration for melphalan should be given on day-2 as follows:

Time	Drug/Hydration	Infusion fluid and volume	Infusion time
-1 hour	Hydration	Sodium Chloride 0.9% 1000mL	30 minutes at 2000mL/hr
-30 mins	Furosemide 20mg IV	N/A	Slow bolus
-30 mins	Hydration	Sodium Chloride 0.9% 1000mL	30 minutes at 2000mL/hr
If urine output <500mL/hr, give second dose of furosemide then recheck urine output			
0 hours	Melphalan	Sodium Chloride 0.9% 500mL	30 minutes at 1000mL/hr
+30 mins	Hydration	Sodium Chloride 0.9% 1000mL	30 minutes at 2000mL/hr
+1 hour	Hydration	Sodium Chloride 0.9% 1000mL	30 minutes at 2000mL/hr

Hydration should only be commenced once the arrival time of melphalan is agreed with pharmacy.

Pre-medication

Prehydration and furosemide prior to melphalan as above
Antiemetics as per local policy

Emetogenicity

Day -7 has high emetic potential
Days -6 to -3 have low emetic potential
Day -2 has moderate emetic potential

Additional supportive medication

Prophylactic antivirals, antibiotics and antifungals as per local policy
PCP prophylaxis upon engraftment only
Mouthwashes as per local policy
Proton pump inhibitor or H2 antagonist as required
Post-transplant GCSF as per local policy
Furosemide PRN for fluid overload
Consider appropriate tumour lysis prophylaxis if disease bulk present

Extravasation

Carmustine is vesicant (Group 5)
Etoposide is irritant (Group 3)
Cytarabine and melphalan are neutral (Group 1)

Investigations – pre first cycle

Investigation	Validity period
FBC	7 days
U&Es (including creatinine)	7 days
LFTs	7 days
Pulmonary function tests	28 days
Echocardiogram	28 days

Other pre-treatment investigations:
ECG
Dental review
Virology screen
Consider formal GFR measurement in those with borderline or impaired renal function

Standard limits for administration to go ahead

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

Investigation	Limit
Creatinine clearance (CrCl)	≥ 60ml/min
ALT	<ULN
Bilirubin	<ULN

Before proceeding the patient's consultant must be satisfied that the patient has adequate cardiac and pulmonary function

Dose modifications

- **Renal impairment**

Consider performing formal renal assessment as part of the patient pre-assessment in those with borderline or impaired renal function. Consider daily recalculation of creatinine clearance using the Cockcroft and Gault equation. In obese patients (body mass index (BMI) ≥30kg/m^2), calculate creatinine clearance using ideal body weight and consider referral for formal GFR evaluation.

Carmustine

Creatinine clearance (mL/min)	Dose
>60	100%
46-60	80%
30-45	75%
<30	Clinical decision (patient unlikely to be fit for transplant)

Etoposide

Creatinine clearance (mL/min)	Dose
>50	100%
15-50	75%
<15	Clinical decision (patient unlikely to be fit for transplant)

Cytarabine – no dose adjustment is necessary

Melphalan

Creatinine clearance (mL/min)	Dose
>30	100%
<30	Contraindicated

- **Hepatic impairment**

Carmustine – no dose adjustment is expected in mild or moderate hepatic impairment - clinical decision. When high doses have been used a reversible hepatic toxicity manifested by increased transaminases, ALP and bilirubin levels has been reported in approx. 1-10% of patients.

Etoposide - If bilirubin <2.5 x ULN with normal albumin and renal function, no dose reduction indicated. If bilirubin >2.5 x ULN **or albumin**<35g/L, consider dose reduction to 50% dose and increase if tolerated.

Cytarabine – clinical decision. The liver apparently detoxifies a substantial fraction of an administered dose of cytarabine. Use with caution and at reduced doses in those with hepatic impairment. Consider dose reduction to 50% where bilirubin > 34 micromols/L.

Melphalan – no dose adjustment necessary

- **Dosing in obesity (BMI ≥ 30kg/m^2)**

Relatively weak data, discuss any dose adjustment for obesity at either the multidisciplinary BMT planning meeting or with the patient's consultant

Drug	Recommendation
Carmustine	Dose on ABW unless weight >120% of IBW then use AdjBW25
Etoposide	Dose on ABW (dose limiting toxicity mucositis)
Cytarabine	Dose on ABW
Melphalan	Dose on ABW (dose limiting toxicity mucositis)

ABW: actual body weight, AdjBW: adjusted body weight, IBW: ideal body weight
AdjBW25 = IBW + 0.25(ABW – IBW)

In obese patients (body mass index (BMI) ≥30kg/m^2), calculate creatinine clearance using ideal body weight and consider referral for formal GFR evaluation.

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 or DOAC 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 comments

Nil

References

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- Krens S D, Lassche, Jansman GFGA, et al**.** Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20:e201-08. Supplementary appendix
- Summary of Product Characteristics – Carmustine (Tillomed Laboratories). Accessed 1 September 2022 via www.medicines.org.uk
- Summary of Product Characteristics – Etoposide (Accord). Accessed 1 September 2022 via www.medicines.org.uk
- Summary of Product Characteristics – Cytarabine (Hospira). Accessed 1 September 2022 via www.medicines.org.uk
- Summary of Product Characteristics – Melphalan (Tillomed Laboratories). Accessed 1 September 2022 via www.medicines.org.uk

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