Clinical Guideline

BONE MARROW TRANSPLANT IN PAEDIATRICS – SUPPORTIVE CARE GUIDELINES

SETTING Stem Cell Transplant and Cellular Therapy Programme, Bristol Royal Hospital for Children

FOR STAFF Medical, nursing and pharmacy staff working in Paediatric Bone Marrow Transplant

PATIENTS Paediatric Bone Marrow Transplant patients

Guidance

This guide should be used in conjunction with the Trust and departmental Standard Operating Procedures (SOPs), the BMT Febrile Neutropenia Guidelines and Antifungal guidelines for Paediatric Haem/Onc/BMT and the patient's individualised protocol.

1. Prophylaxis

1.1 ANTI-INFECTIVES

i. Antibiotics

AGENT	INDICATION	DOSE	NOTES
Ciprofloxacin	Start once neutrophils <0.5 x10^9/L	1 month – 18yrs 7.5mg/kg (max 500mg) po BD Tablet: 250mg, liquid. Omit if patient unable to swallow.	History of C.diff discuss with consultant. Stop if on IV antibiotics or when neutrophils >0.5 x10^9/L for 2 consecutive days Switch to penicillin V once patient engrafted.
Phenoxymethylpenicillin (Penicillin V)	Start once engrafted	< 1 yr: 62.5mg po BD 1-5yrs: 125mg po BD 5 yrs+: 250mg po BD	Avoid if penicillin allergy Stop if on IV antibiotics Lifelong treatment Tablets 250mg, liquid available
Azithromycin	Toxoplasma positive donor/recipient Alternative if allergic to penicillin	10mg/kg M/W/F Max 500mg per dose Tablets and liquid	Start at admission. Continue until able to take co-trimoxazole. (Penicillin prophylaxis not required whilst on azithromycin) Continue lifelong if pencillin allergic Caution- prolong QT interval

ii. Antifungals

AGENT	INDICATION	DOSE	NOTES
See Antifungal guidance for Paediatric Haem/Onc/BMT			Stop once off immunosuppression, immune recovery with CD4> 300. , no cytopenia and no evidence of active fungal infection.

iii. *Pneumocystis Jirovecii* Pneumonia (PCP) prophylaxis

AGENT	INDICATION	DOSE	NOTES
Co-trimoxazole	1st line	Take PO BD Saturday & Sunday <0.5m^2:24mg/kg 0.5-0.75m^2: 240mg 0.76-1.m^2: 360mg 1-1.5m^2: 480mg >1.5m^2: 960mg	Commence post-transplant (D+28) when platelets>50x10^9/L and neutrophils >1x10^9/L Continue at least for 6 months post- transplant and based on immune recovery = CD4>300
Folic Acid	For patients on co-trimoxazole	<1 yrs: 500micrograms/kg (max 5mg) po on Mondays only 1-18yrs: 5mg on Mondays only	
Pentamidine	Patients intolerant/unable to have co-trimoxazole e.g. Nil by mouth, not engrafted	Intravenous: 4mg/kg (max 300mg) IV every 4 weeks. Nebulised: 5yrs$^+$: 300mg every 4 weeks.	Order through pharmacist. Requires 48hours notice. For use when platelets <50 x10^9/L, or neutrophils <1 x10^9/L.
Atovaquone	3nd line (discuss with consultant)	1month + 30mg/kg po OD (max 1500mg/day)	Take with high fat food to aid absorption
Dapsone	Discuss with consultant as option if above not appropriate	1 month -18 yrs; 2mg/kg (max 100mg) po OD	Increased risk of haemolysis and methaemoglobinaemia

iv. Antivirals

AGENT	INDICATION	DOSE	NOTES
Aciclovir	Herpes Simplex Virus prophylaxis	Start Day -4 < 1yr: 200mg po BD 1-12yrs: 400mg po BD >12yrs: 400mg po TDS If PO not possible: 3 months-12yrs: 250mg/m^2 IV TDS >12yrs: 5mg/kg IV TDS	Not varicella zoster prophylaxis Switch to IV if PO not tolerated Stop prophylaxis if on other antivirals. IV - Use ideal body weight for obese patients. Continue for 1 year post-transplant

Ganciclovir	Cytomegalovirus (CMV) infection	Dosage and Administration of Ganciclovir	Made in Pharmacy production order through pharmacist Obtaining out of hours: Obtaining and Administering Ganciclovir Out of Hours
Foscarnet	CMV infection	Dosage and Administration of Foscarnet	Made in Pharmacy production order through pharmacist
Cidofovir	CMV or adenovirus infection	Dosage and Administration of Cidofovir	Nephrotoxic: Prescribe probenecid and hydration Made in PSU order through pharmacist.
Immunoglobulins (Privigen®)	Hypogammaglobulinaemia/ infection >6months despite infection. Following current NHSE guidance for indication	Dosage and Administration of Human Intravenous Immunoglobulin (Privigen) and clinical guideline: Human Intravenous Immunoglobulin (Privigen 100mg/ml®) Start on D+1 every 4 weeks if evidence of hypogammaglobulinaemia	Requires intravenous immunoglobulin (IVIG) electronic form to be completed on Medway:

1.2 GRAFT VERSUS HOST DISEASE (GVHD) PROPHYLAXIS

AGENT	INDICATION	DOSE	NOTES
Ciclosporin	Usually from day-3 pre-transplant	IV (Sandimmun):2.5mg/kg 12hrly PO (Neoral): 1.5 times IV dose BD	Convert to oral ciclosporin (Neoral) when able to tolerate oral medication Monitoring required See SOP:
Tacrolimus	Second line to ciclosporin	Dosage and Administration of Tacrolimus for Paediatric BMT Patients Note may be switched to BD dosing for treatment GVHD: 0.015mg/kg IV BD Run over 2 hours (seek pharmacist for dosing info)	Requires therapeutic levels
Mycophenolate Mofetil (MMF)	Monotherapy or additional therapy	**IV & PO: 1 month-18yr:** 15mg/kg TDS	Tablets/capsules 250mg and 500mg. Liquid available. Use cytotoxic precautions when preparing.

			IV doses require ordering through production
Methotrexate (low-dose)	Day +1 post-transplant as part of patients treatment plan	Low Dose Methotrexate for GVHD Prophylaxis	Low Dose Methotrexate for GVHD Prophylaxis
Alemtuzumab (Campath)	As per conditioning protocol	Administration of Alemtuzumab (Campath)	Requires ordering through Campath Access Program (named patient basis). Additional ordering requirement -Need 1 week notice
Rabbit Anti-Thymocyte Globulin (ATG)	As per conditioning protocol	Rabbit Anti-Thymocyte Globulin (ATG) thymoglobuline Dosing and Administration	Note brand specific Additional ordering requirements need 1 week notice

1.3 VENO-OCCLUSIVE DISEASE TREATMENT/PROPHYLAXIS

AGENT	INDICATION	DOSE	NOTES
Ursodeoxycholic acid	From admission until day +30/discharge	**1 month+** 10mg/kg/ BD Orally (Round to nearest capsule if relevant) Caps/tabs: 150mg and 250mg+ liquid available	Indicated in full intensity transplants and in reduced intensity transplants associated with an increased risk of hepatic toxicity (busulfan containing regimen or previous history of abnormal liver function tests) Consider increasing the dose to 15mg/kg three times a day if raised bilirubin.
Defibrotide	Severe diagnosed VOD	1 month+ 6.25mg/kg IV QDS Vials: 200mg CIVAS available	Requires meeting NHS E clinical commissioning policy criteria and completing Blueteq form for approval before issuing. Nursing Management of Patients Diagnosed with Post Hematopoietic Stem Cell Transplant Veno-Occlusive disease (VOD) Clinical Guideline Hepatic Veno-Occlusive Disease in Haematology and Oncology Patients

1.4 TUMOUR LYSIS SYNDROME PROPHYLAXIS

Only for patients with malignancy that is not in complete remission.

AGENT	INDICATION	DOSE	NOTES
Allopurinol	Prophylaxis	**1 month-18yrs;** 100mg/m2 (max 100mg) TDS	Start with first day of conditioning chemotherapy and continue for 5 days Caution and dose reduction in acute kidney injury
Rasburicase	If allopurinol not tolerated or uric acid elevated despite allopurinol therapy	**From 1 month;** 200micrograms/kg OD Vials 1.5mg (Round to nearest size if possible)	Avoid in G6PD deficiency Give over 30 minutes

2. Antiemetics

See Antiemetics Guidelines for Paediatric Patients Receiving Chemotherapy and review at day +1 post-transplant.

3. Supportive Care for Specific Conditioning Agents

3.1 BUSULFAN

AGENT	INDICATION	DOSE	NOTES
Clonazepam	Antiepileptic prophylaxis whilst having busulfan	Start 24 hours pre busulfan dose: **1 month-12yrs;** 12.5micrograms/kg (max 500 micrograms) BD **>12yrs;** 500 micrograms BD	Continue until 48 hours after last dose

4. Management of Graft versus Host Disease (GvHD)

4.1 TOPICAL TREATMENT

AGENT	INDICATION	DOSE	NOTES
Emollin Spray	Topical emollient	Spray lightly over body 2 – 3 times a day	Avoid eyes Warning: flammable risk
Zerobase cream	Topical emollient	Apply liberally when required	Apply immediately after bathing/showering Use a clean spoon to reduce contamination Apply in direction of hair growth to avoid folliculitis

Hydromol ointment	Topical emollient	Apply liberally when required	(See notes above)
Dermol lotion	Soap substitute	Use as a soap substitute	
Hydrocortisone 1%	Mild steroid	Apply thinly to affected area(s) (usually face) BD Cream/ointment available	May be used more often in severe GVHD Usually applied to face
Eumovate (clobetasone butyrate 0.05%)	Moderate potency steroid cream	Apply thinly to affected area(s) BD Cream/ointment available	May be used more often in severe GVHD. Usually applied to body (severe cases to face)
Betnovate ***(Betamethasone valerate 0.1%)***	Potent topical steroid	Apply thinly to affected area(s) BD Cream/ointment available	May be used more often in severe GVHD
Tacrolimus (topical)	Moderate Severe GVHD Calcineurin inhibitor	Apply to the affected area(s) BD	Two strengths available 0.03% and 0.1% ointment

4.2 STEROID MANAGEMENT OF GASTROINTESTINAL GVHD

AGENT	INDICATION	DOSE	NOTES
Budesonide	Gastrointestinal GVHD	>/= 8yrs: 3mg TDS PO <8 years: not recommended	Local effect and limited absorption Absorbed past stomach in pH >6.4 Do not crush capsules
Prednisolone	GVHD	Usual dose 1-2 mg/kg daily PO	Give as single or twice daily dose.
Methylprednisolone	GVHD	Convert from oral pred dose or start at 1-2mg/kg	Switch to oral prednisolone when appropriate

5. Additional drug dosing

AGENT	INDICATION	DOSE	NOTES
Lenograstim (Granulocyte Colony Stimulating Factor, G-CSF)	See Use of Granulocyte Colony Stimulating Factor (G-CSF) in Post-Transplant Patients	S/C: IV 5 micrograms/kg (max 263 micrograms)	Use of Granulocyte Colony Stimulating Factor (G-CSF) in Post-Transplant Patients
Tramadol	Pain	>1 year: 1 mg / kg 4-6 hourly (IV/PO) (Max 100 mg/dose and 400 mg/day)	Clinical Guideline: Paediatric Acute Pain Management
Esomeprazole	Gastro-oesophageal reflux disease (presence of erosive reflux oesophagitis)	Granules: 10-20kg: 10mg OD >20kg: 20mg OD 12-18yrs: 40mg OD IV:1-11months: 1mg/kg OD (max 10mg) 1–11yrs (10kg+): 10mg IV OD 12-17yrs: 20mg IV OD	Use for patients with nasogastric tubes only Stop on discharge unless symptoms present or platelets < 50 x10^9/L
Omeprazole	Gastro-oesophageal reflux disease (presence of erosive reflux oesophagitis)	<10kg: 700micrograms/kg. Increase if needed to up to 3mg/kg (Max 20mg daily) 10-20kg: 10mg (Max 20mg daily) >20kg: 20mg (Max 40mg daily) Round to nearest 2.5mg.	For patients able to swallow

REFERENCES	UpToDate, 2017. Pentamadine (oral inhalation): Drug information: Available at: https://www.uptodate.com/contents/pentamidine-oral-inhalation-drug-information?source=preview&anchor=F44486490#F44486490 [Accessed 11th October 2017] Ho VT, Revta C, Richardson PG et al. 2008. Hepatic veno-occlusive disease after hematopoietic stem cell transplantation: update on defibrotide and other current investigational therapies. Bone Marrow Transplant; 41:229-237 Larson R, Pui C, 2017. Tumor Lysis syndrome: prevention and treatment. Available at: https://www.uptodate.com/contents/tumor-lysis-syndrome-prevention-and-treatment?source=search_result&search=tumor%20lysis%20syndrome%20allopurinol&selectedTitle=1~150#H21712058 [Accessed 18th October 2017] Peniket A. 2017. Guidelines for Diagnosis and Management of Cutaneous Graft-Versus-Host Disease. Oxford University Hospital NHS Foundation Trust. Available at: http://nssg.oxford-haematology.org.uk/bmt/gvhd/B-2-7c-diagnosis-and-management-cutaneous-gvhd.pdf#:~:text=Guidelines%20for%20Diagnosis%20and%20Management%20of%20Cutaneous%20Graft-Versus-Host,in%20Haematology%20GVHD%20guidelines%20recommend%20organ-specific%20management%20and [Accessed 18th October 2017] Evelina London Paediatric Formulary, Available online: http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80 [Accessed 23rd October 2020 Guidelines for the prophylaxis of *Pneumocystis Jirovecii* Pneumonia (PJP) in children with solid tumours. Nov 2016 https://www.cclg.org.uk/write/MediaUploads/Member%20area/Treatment%20guidelines/PJP_Prophylaxis_Guideline_Final.pdf Skeens et al. Twice daily IV bolus tacrolimus infusion for GVHD prophylaxis in children undergoing stem cell transplantation Bone Marrow Transplantation (2012) $7: 1415-1418
RELATED DOCUMENTS AND PAGES	Antifungal guidance for Paediatric Haem/Onc/BMT Antiemetics Guidelines for Paediatric Patients Receiving Chemotherapy Dosage and Administration of Ganciclovir Dosage and Administration of Foscarnet Dosage and Administration of Cidofovir Dosage and Administration of Human Intravenous Immunoglobulin (Privigen) Human Intravenous Immunoglobulin (Privigen 100mg/ml®) Obtaining and Administering Ganciclovir Out of Hours Dosage and Administration of Tacrolimus for Paediatric BMT Patients

	Low Dose Methotrexate for GVHD Prophylaxis Administration of Alemtuzumab (Campath) Rabbit Anti-Thymocyte Globulin (ATG) thymoglobuline Dosing and Administration Nursing Management of Patients Diagnosed with Post Hematopoietic Stem Cell Transplant Veno-Occlusive disease (VOD) Hepatic Veno-Occlusive Disease in Haematology and Oncology Patients Use of Granulocyte Colony Stimulating Factor (G-CSF) in Post-Transplant Patients Clinical Guideline: Paediatric Acute Pain Management
AUTHORISING BODY	Paediatric Haematology, Oncology and Bone Marrow Transplant Quality Assurance Forum (Quaf)
SAFETY	No additional safety concerns
QUERIES AND CONTACT	BMT Registrar: [redacted] Oncology Registrar: [redacted] Haematology Registrar: [redacted] For out of hours requests contact via switchboard. BMT/Haematology/Oncology Pharmacists: [redacted]