

Total Lymphoid Irradiation (TLI)/Rabbit Anti-Thymocyte Globulin (rbATG) For Non-myeloablative Allograft

Summary of Schedule

Date:

Day														
DRUG	-12	-11	-10	-9	-8	-7	-6	-5	-4	-3	-2	-1	0	+1
Admission	*													
Total Lymphoid Irradiation (TLI) <i>Radiation treatment</i>		*	*	*	*	*			*	*	*	*		
Methylprednisolone <i>To minimise reactions to rbATG</i>	*	*	*	*	*	*								
Rabbit ATG (rbATG) <i>Antibody to suppress immune system</i>		*	*	*	*	*								
Pentamidine <i>Prevents a specific pneumonia called PCP</i>														*
Bone marrow/stem cell infusion													*	
Ciclosporin <i>Continues to suppress immune system</i>										*	*	*	*	*
Mycophenolate mofetil <i>Continues to suppress immune system</i>										*	*	*	*	*
Ondansetron (O) Metoclopramide (M) Dexamethasone (D) <i>Different types of anti-sickness</i>		O M	O M	O M	O M	O M	O M	O M	O M D	O M D	O M D	O M D	O M	

INDICATIONS

Advanced stage cutaneous T cell lymphoma

This protocol will be rarely used in Oxford and is intended only for patients under the care of a specialist centre elsewhere who will be treated with Total Skin Electron Beam Radiation Therapy (TSEB). Transplant scheduling will be as discussed with the centre giving TSEB.

Pre-assessment

- Ensure pre-transplant investigations are carried out as per Checklist/Record B3.10b
- Ensure patient has a double lumen central line in situ.
- Ensure results of pre-transplant investigations are checked by a Haematology SpR and recorded on Checklist/Record B.3.10b and filed in patient medical records
- Ensure patient consent has been obtained
- Haematology SpR to complete electronic BMT front sheet and email to BMT Administrator to distribute and file in patient record
- Prescribe chemotherapy and supportive treatment at least 5 days before admission
- Send NHSBT referral form at least one working day before the start of patient conditioning and ensure a copy is placed in the medical notes.
- Ensure donor clearance is obtained, reviewed and documented in recipient's notes prior to admission
- Ensure that patient receives irradiated blood products from the start of conditioning and indefinitely thereafter.
- Day - 11 ensure pregnancy test is carried out on all women of child-bearing potential unless they have been sterilized or have undergone a hysterectomy.

CHEMOTHERAPY AND FLUIDS

Pre-TLI		
	TSEBT (Total Skin Electron Beam Therapy)	100 cGy (4x/week) for extensive skin involvement (off site)
Day -12 20.00	Methylprednisolone	1mg/kg iv infusion in 100mls sodium chloride 0.9% over 30 minutes.
Day –11 to –7		
am	TLI	One TLI fraction (80cGy) in the morning. Check exact time with radiotherapy dept.
11.30	Methylprednisolone	1mg/kg iv infusion in 100mls sodium chloride 0.9% over 30 minutes. To be commenced 30 minutes before rATG
	Chlorphenamine Paracetamol	10mg iv bolus 30 mins pre rbATG 1g po 30 mins pre rbATG
12.00	Rabbit ATG (Thymoglobulin)	1.5mg/kg iv od in 500ml sodium chloride 0.9% OVER 8 hours through a 0.22 micron filter. Each ATG dose must be completed within 18 hours of being made up. There is no need to perform a separate test dose but: For the first two hours of the first dose a doctor must be present at all times on the ward. Adrenaline, chlorphenamine, hydrocortisone should be drawn up and available at the bedside.
20:00	Methylprednisolone	1mg/kg iv in 100ml sodium chloride 0.9% over 15 minutes
Day –4 to -2		
am	TLI	One TLI 80 cGy fraction in the morning. Check exact time with radiotherapy dept.

Day -1		
am/pm	TLI	One TLI fraction (80 cGyx2) in the morning and one in the evening. Check exact time with radiotherapy dept.
Day 0		
06.00		1000ml sodium chloride 0.9% over 6hrs
12.00	Marrow/PBSC infusion	Give hydrocortisone 100mg iv, chlorphenamine 10mg iv 30 minutes before cell infusion.
Day +1		
	Pentamidine	4mg/kg/day/iv (max 300mg) in 100ml sodium chloride 0.9% over 1 hour

Note:

From Day +28 some patients, with persistent Sezary cells, may receive ECP but this will be decided on a patient by patient basis.

ADMINISTRATION OF rATG: Refer to nursing care plan N.6a

BONE MARROW/STEM CELL INFUSION: Refer to nursing care plan N.51 or N.18

ANTI-EMETICS Since TLI can cause nausea; make sure adequate antiemetic therapy is prescribed.

Day -11 to -1	Metoclopramide 20mg iv/po qds Ondansetron 8mg po/iv/bd
Day - 4 to -1	Dexamethasone 4mg po/iv pre TLI
Day 0	Ondansetron 8mg po/iv/od Metoclopramide 10mg iv/po tds-qds PRN

CONCURRENT MEDICATION

Norethisterone	5-10mg po tds from day 0 until platelets $>50 \times 10^9/l$ (menstruating women only)
Antifungal prophylaxis	Refer to Antifungal protocol. Start from day 0 until neutrophils $>1.0 \times 10^9/l$ (or longer if on steroids) http://nssg.oxford-haematology.org.uk/general-clinical-management/H-94-antifungal-therapy-guidelines.pdf

Aciclovir	For CMV Prophylaxis If either donor or recipient or both are CMV + then: 500mg /m ² tds iv or 800mg po qds day -7 to day +30 then 800mg po qds for 3 months, then 200mg tds for further 3 months if VZV positive
Ciclosporin	Start orally on Day -3. Refer to protocol http://nssg.oxford-haematology.org.uk/bmt/clin-man/B-2-19-ciclosporin-for-patients-allogenic-bmt.pdf
Mycophenolate mofetil (MMF)	1g tds po from Day 0 (at 5-10 hours after stem cell infusion is complete). Can be given via intravenous infusion if po not tolerated (If renal failure and GFR < 25ml/min do not exceed dose of 1 gm bd. No dose adjustment for liver disease). MMF dosing to be monitored and altered as clinically appropriate. Stop MMF at Day 28 for sibling donors. Taper MMF for unrelated donors from day +40 by 10% weekly until discontinued: this will usually be around Day +96
Pentamidine	4mg/kg/day (max 300mg) iv on day+1 and day +30 (unless started on co-trimoxazole).
Ursodeoxycolic acid	See VOD protocol http://nssg.oxford-haematology.org.uk/bmt/clin-man/B-2-12-vod-management.pdf
Omeprazole	20mg od from start of conditioning until platelet count >50x10 ⁹ /l
Allopurinol	300mg po od whilst patient has TSEBT (on discretion of off site treatment team). Consider during TLI and ATG if necessary.

INVESTIGATIONS

Daily	FBC, creatinine, urea & electrolytes, liver function, weight, urinalysis
Mon/Thurs	clotting, calcium, magnesium, phosphate
Mon/Fri	Group and screen
Monday	Ciclosporin levels - trough level. 200 – 300 ng/l CMV PCR from Day+1 EBV PCR weekly from Day +1
Other	Chest X-ray weekly and as clinically indicated Other specimens for virology as clinically indicated.

MEDICATION ON DISCHARGE (TTOs)

Norethisterone	Stop when platelets >50 x 10 ⁹ /l
Antifungal Prophylaxis	Refer to Antifungal protocol. Stop when neutrophils >1x 10 ⁹ /l (may be longer if patient on steroids)
Co-trimoxazole	480mg po daily Mon, Wed, Fri: start when neutrophils >1x10 ⁹ /l and continue until one month after immunosuppressive therapy stopped. Then increase to 960mg when counts stable. If allergic to co-trimoxazole, Pentamidine 4mg/kg iv(max dose 300mg) monthly
Aciclovir	Refer to concurrent medications in this protocol.

Omeprazole	Stop when platelet count $>50 \times 10^9/l$ unless clinically indicated
Ciclosporin (Generic)	See protocol. Check with consultant or registrar.
Penicillin V	250mg BD for life. Erythromycin if penicillin allergic

References

Thymoglobulin 25mg powder for solution for infusion - Summary of Product Characteristics. Last updated on eMC 03-Oct-2016.

Stanford Trial Protocol: Wen-Kai Weng et al. A Phase II Study of Non-myeloablative Allogenic Transplantation using Total Lymphoid Irradiation (TLI) and Antithymocyte Globulin (ATG) in Patients with Cutaneous T Cell Lymphoma. Revision 3 March 2010. Stanford Cancer Centre.

Audit

These processes are subject to the OxBMT audit programme

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Circulation

NSSG Haematology Website

Name	Revision	Date	Version	Review date
	New Document	Sept 17	1.0	Sept 19
Denise Wareham, BMT Nurse Coordinator	Addition of day -12 methylprednisolone	Oct 17	1.1	Sept 19
Dr Andy Peniket BMT Consultant Lead	MMF modifications And minor amendments	Apr 2018	1.2	Apr 2020