UK Clinical Community Consensus on the Emerging use of Post-Transplant Cyclophosphamide (PTCy) in Allogeneic Stem Cell Transplant

Consensus Statement
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Introduction

This consensus statement represents a response to emerging data relating to the increasingly important role of post-transplant cyclophosphamide (PTCy) as a graft versus host disease (GvHD) prophylaxis regimen in patients transplanted using matched and mismatched unrelated donors. It is intended to support UK transplant centres prior to publication of further evidence such as the results of the Methods of T Cell Depletion (MoTD) study, and will form the basis of a full clinical guideline in the future.

The use of PTCy for GvHD prophylaxis in unrelated donor transplant was discussed at a symposium convened by the UK Stem Cell Strategic Forum. This consensus has been developed following the symposium, and has been collaboratively drafted by representatives from UK allogeneic stem cell transplant centres, the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT), the UK Aligned Registry and the UK Stem Cell Strategic Forum. It is informed by expert opinion and prevailing clinical practice.

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Clinical guidance

1. The BSBMTCT will regularly update this rapid consensus statement in response to emerging evidence. The BSBMTCT will develop detailed clinical guidance, including specific guidance for paediatric and adult non-malignant patients in the near future.

2. The British Society for Histocompatibility and Immunogenetics (BSHI) will develop guidelines on appropriate donor search and selection approaches and the management of patients with donor-specific antibodies undergoing mismatched transplant in the era of PTCy.

Clinical Trials and Data Collection

3. Whenever possible, patients should be enrolled into national clinical trials on the use of PTCy, for example the MoTD trial.

4. The UK clinical transplant community should establish future clinical trials to further improve the outcomes of PTCy for the prevention of GvHD.

5. The UK clinical transplant community should develop clinical trials to investigate the use of PTCy in paediatric patients.

6. The UK clinical community should develop clinical trials further investigating the use of PTCy in non-malignant settings.

7. All cases using PTCy-based GvHD prophylaxis outside of a clinical trial should be reported, according to routine practice, to the BSBMTCT registry. This should include long-term outcomes following treatment, including all instances of infection, transplant-related toxicity, and relapse.

8. Consideration should be given to the collection of a prospective dataset, with matched biological samples, in patients transplanted using PTCy, with the aim of generating granular UK specific data and supporting pivotal translational studies. This will be facilitated by the UK Stem Cell Strategic Forum Data Commission working with the BSBMTCT and other interested parties including basic scientists.

9. The UK Aligned Registry should collect search request data to support the UK community to understand changing practice.

Patient selection

10. PTCy can be considered as an option for GVHD prophylaxis for patients undergoing allogeneic transplant:
    - Aged 18 and over; with a haematological malignancy in whom transplant is indicated (including acute myeloid leukaemia, myelodysplasia, chronic myeloid leukaemia, chronic myelomonocytic leukaemia, acute lymphoblastic leukaemia, lymphoma, myelofibrosis, and myeloma)
    - Aged under 18; for any transplant indication

11. At present, additional data is required to make any formal recommendations on the use of PTCy GvHD prophylaxis in patients
    - Aged 18 and over with a non-malignant indication for transplant

Donors and Donor selection

12. Transplant centres should actively consider that PTCy prophylaxis may be of particular importance in improving outcomes and access to donors for patients from mixed and minority ethnic backgrounds, where currently access to unrelated donor transplant is challenging. Data from international groups also indicates that a PTCy-based approach may also increase the speed of donor identification and time to transplant.

13. PTCy GvHD prophylaxis may be used in the treatment of patients undergoing allogeneic stem cell transplant using any of the following donors:
    - Haploidentical related donor (5/10 HLA match)
    - Mismatched related donor (9/10 or lower HLA match)
    - Mismatched unrelated donor (9/10 or lower HLA match)

14. Until the results of the MoTD trial are available PTCy GvHD prophylaxis may be considered an effective option in the treatment of patients undergoing allogeneic stem cell transplant using any of the following donors:
    - Fully matched related donor (10/10 HLA match)
    - Fully matched unrelated donor (10/10 HLA match)

15. All patients should be screened pre-transplant for donor specific anti-HLA antibodies at the point of donor search, avoiding HLA-mismatches with specificity against clinically relevant antibodies. Screening for donor-specific antibodies should continue for a minimum of 30 days prior to transplant.

16. Consideration should be given to the use of HLA selected platelets in patients using alternate donors if they have donor-specific antibodies. There is currently no data available to direct this practice and it is an ongoing area of investigation.

17. When using an HLA-mismatched donor with PTCy, there is insufficient evidence currently to recommend at which HLA-loci the mismatch is preferred.

18. When selecting unrelated donors for use with PTCy, it is recommended, on the basis of the available published data, to use:
    - A donor with age <35yrs old
    - A cytomegalovirus (CMV) IgG matched donor

19. In patients in whom it is predicted that rapid identification of a well matched unrelated donor will be challenging, all potential donor sources should be considered, and donor searches should be performed concurrently for all donor types (Lee *et al*). The Contemporary Guidelines from the NMDP/CIBMTR (Jimenez-Jimenez *et al*, 2025) are a useful reference and have been adapted for the UK context overleaf.

20. Searches for alternative donors, in patients in whom it can be predicted that identification of a well matched unrelated donor will be challenging, should be performed as early as possible (ideally within 48 hours of decision to transplant), particularly for high risk indications where it is important to reduce time to transplant.

21. Given the potential increase in available door options when using PTCy-based GvHD prophylaxis, consideration should be given to optimising donors based on younger age, CMV status, and other clinical factors of importance.

Donor cell donor selection guidelines
Adapted for the UK from the NMDP/CIBMT Guidelines (2025)

Perform early testing

- Minimum high-resolution HLA typing on patient at HLA-A, -B, -C, -DRB1, -DQB1 and -DPB1
- HLA antibody testing on patient
- HLA typing on family members

Begin preliminary search via the UK Aligned Registry to evaluate unrelated and related donors simultaneously

Suitable matched sibling donor available?

YES

Proceed to transplant

NO

10/10 matched unrelated donor (MUD) very likely available?

Not sure if a 10/10 MUD is likely available?

- If search results are clearly good or poor, proceed below accordingly
- If search results are questionable, explore both MUD and alternative donor paths below concurrently
- If you need more help contact the UKAR for guidance

YES

Proceed to HCT: favour younger age (<35) without donor specific antibodies (DSAs).

NO

Proceed with preferred alternative donor

Mismatched unrelated donor (MMUD)

• Favor younger age (<31) without DSAs

•Additional donor attributes should be evaluated with donor availability in an approach that is individualized to the patient

•Secondary characteristics:

–ABO matching may reduce post-HCT transfusion burden

–Donor CMV serostatus may be considered in specific clinical cases (e.g., SCID)

–Avoid large patient/donor weight discrepancies in bone marrow HCT

Haploidentical donor (haplo)

• Favor younger age (<31) without DSAs

•DRB1 mismatch may minimize relapse

•DPB1 TCE non-permissive mismatch may be associated with better survival

• For support with decision-making refer to the haplo predictor tool developed by Fuchs et al, 2021 (link)

• For additional considerations refer to EBMT recommendations - Ciurea et al., 2020 (link)

Umbilical cord blood (UCB)

•HLA match: minimum 4/6 match (HLA-A and -B antigen, -DRB1 allele) and minimum 4/8 match (HLA-A, -B, -C, -DRB1 allele)

•Consult Anthony Nolan / NHSBT Cord Support Program: Cord Blood Unit (CBU) Flow Chart.

• For free assistance in CBU shortlisting, email cordsupport@anthonynolan.org.

Graft source

22. PTCy GvHD prophylaxis is suitable for use with peripheral blood stem cells (PBSC) or bone marrow (BM)-derived donor cells

23. PTCy GvHD prophylaxis is not recommended for use with umbilical cord blood.

24. PTCy GvHD prophylaxis is suitable for use with fresh or cryopreserved cells.

25. The recommended target CD34+ cell dose for PTCy-based regimens in adult recipients is a minimum of 4×10^6 per kilogram of actual body weight, based on recent clinical trials.

Conditioning regimens

26. PTCy GvHD prophylaxis is suitable for use with both myeloablative (MAC) and reduced intensity conditioning (RIC) regimens

PTCy dosing and schedule

27. The current PTCy dosing recommendation is 50 mg/kg cyclophosphamide once daily (based on Ideal Body Weight) on days +3 and +4 after HSCT.

28. Cyclophosphamide should be given as IV infusion (over 1-2 hours depending on volume, according to standard transplant centre practice).

29. Hydration (pre and post-cyclophosphamide) and Mesna administration should be given as per standard transplant centre practice.

30. Systemic immunosuppressive agents (including corticosteroids as anti-emetics) should not be given until at least 24 hours after the completion of PTCy.

31. Azole (e.g. posaconazole) should be delayed from beginning of conditioning through to completion of D+4 PTCy to avoid potential drug-drug interactions with cyclophosphamide.

Cautions

32. PTCy-based GvHD prophylaxis should be used with caution in patients with known cardiac dysfunction.

33. Cytokine release syndrome (CRS) is a recognised rare complication of PTCy-based GvHD prophylaxis and should be managed according to standard transplant centre practice.

Patient consent and decision-making

34. Patients and family members should be actively involved in decisions about their treatment and provided with meaningful opportunity to discuss all treatment options prior to proceeding with PTCy-based prophylaxis.

35. Patients should be counselled on the potential impact on fertility and opportunities for fertility preservation should be offered, as per standard practice in allogeneic transplantation.

Quality

36. Transplant centres delivering PTCy based prophylaxis should be fully compliant with the latest JACIE standards and have suitable data and quality management and reporting capabilities.

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