

Adoptive Immunotherapy with CD25/71 allodepleted donor T cells to improve immunity after unrelated donor stem cell transplant

Randomised phase II trial for patients with haematological malignancy undergoing unrelated donor PBSCT with Alemtuzumab based conditioning. The primary objective is to assess whether adoptive immunotherapy with CD25/71 allodepleted donor T-cells can be safely used to improve T-cell reconstitution after unrelated donor SCT.

Trial design

Patients randomised 2:1 in favour of those receiving the ATIMP (CD25/71 allodepleted donor T-cells), compared with a control group receiving standard of care therapy.

Patients randomized to the ATIMP arm will undergo an unstimulated leucapheresis for generation of mature DC two weeks prior to SCT. A week later donor will either undergo unstimulated leucapheresis or a 500ml whole blood draw for the generation of PBMC. The isolated donor PBMC will then be co-cultured with the irradiated recipient mature DC and allodepletion performed using immunomagnetic CD25/71 negative selection (CliniMACs system).

Patients who have engrafted with no acute GVHD >Grade I will be infused with increasing doses of the allodepleted donor T cells (10^5 /kg at day 30, 3×10^5 /kg at day 60 and 10^6 /kg at day 90 post-SCT until either their CD3 count is normal ($>700/\mu\text{L}$) or they develop acute GVHD > GrI.

Patients in the control arm will receive identical supportive care, but will not receive the ATIMP. Patients in both arms of the trial will be followed up until 1 year post-SCT.

Trial end points

Primary endpoint:

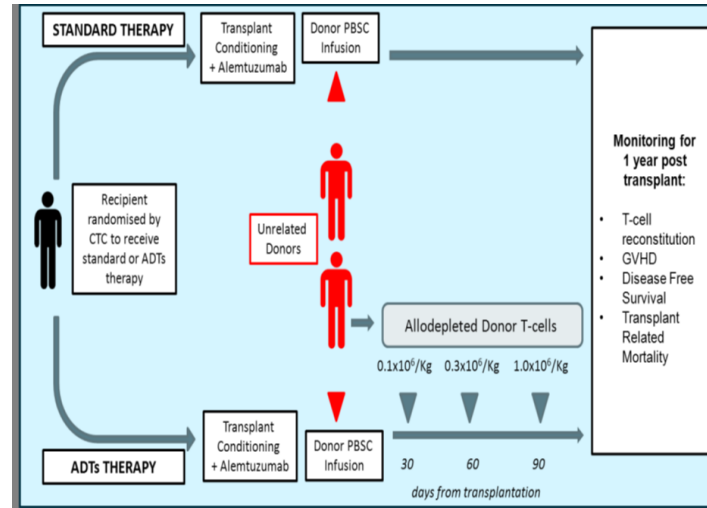
CD3+ve T cells at 4 months post-SCT

Secondary endpoints:

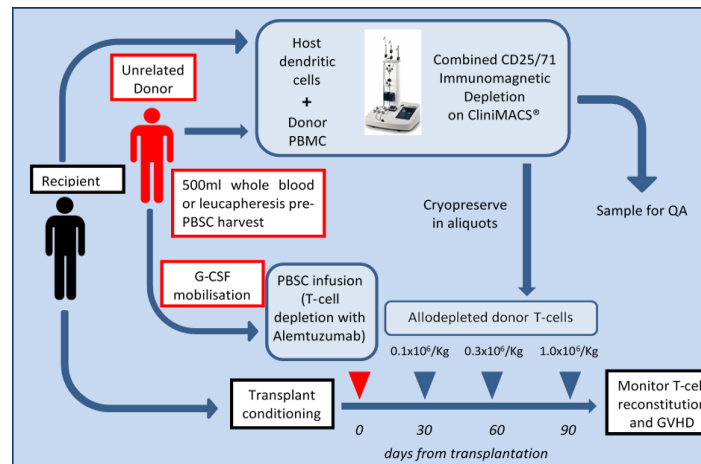
- Incidence of grade II-IV acute & chronic GVHD
- Time to recovery of normal T-cell ($>700/\mu\text{L}$) & CD4 ($>300/\mu\text{L}$) & normal TCR diversity
- In vitro* anti-viral responses of circulating PBMC
- Transplant related mortality/disease-free survival at 1 year post-SCT

Trial outline

Allodepleted Donor T-cells Therapy vs Standard Therapy



Summary of Allodepleted Donor T-cells Therapy



Eligibility Criteria

Patient Inclusion Criteria

- Age ≥ 16 years
- Underlying haematological malignancy
- Planned allogeneic PBSCT from a 9/10 or 10/10 HLA-matched unrelated donor, using an Alemtuzumab-based conditioning protocol
- Written Informed consent

Patient Exclusion Criteria

- Life expectancy < 6 weeks
- Female patients who are pregnant and lactating
- Serologically positive for Hep B, C or HIV pre-SCT

Patients will not be eligible for infusion of the ATIMP if they have:

- Engraftment failure
- Acute GVHD > Grade I
- Require supplemental oxygen
- Severe intercurrent infection
- Liver derangement
- Circulating T Cell $>700/\mu\text{L}$

Donor Inclusion Criteria

- Donors must be unrelated to and HLA-matched (10/10) or a single antigenic/allelic mismatch(9/10)
- Donors must be healthy and pass a medical examination that they are fit to donate PBSC
- Donors must sign an informed consent form indicating that they are aware their additional donation of PB or leucapheresis is for research

Donor Exclusion Criteria

- Donor registry determines contraindication to donate mobilised peripheral blood stem cells, 500ml peripheral blood draw or unstimulated leucapheresis for PBMC

Sample size: 24 patients (16 in ATIMP arm and 8 in Control arm)