A PHASE 1/2 STUDY OF THE USE OF IMATINIB IN PATIENTS UNDERGOING REDUCED INTENSITY ALLOGRAFTING FOR CHRONIC MYELOID LEUKAEMIA.

Background:

The curative potential of allogeneic stem cell transplantation (SCT) in CML is limited by two main factors: the toxicity of the conditioning regimen and graft-versus-host disease (GVHD). The advent of reduced intensity conditioning regimens (mini-allografts) using concurrent T cell depletion (TCD) has allowed allogeneic SCT to be contemplated in many patients in whom transplantation using a conventional regimen is currently contra-indicated. The success of such regimens are however dependent on the use of donor lymphocyte infusions which can be associated with severe GVHD if used early after transplantation. Using Imatinib can control the disease in the early post transplant period and DLI therapy can be implemented at twelve months post SCT.

Aims:

Main objective:

- To assess the safety and tolerability of adjunctive Imatinib in patients with CML in 1st Chronic Phase undergoing a reduced intensity allogeneic stem cell transplant

Secondary objective:

- To assess the anti-leukaemic activity of a reduced intensity allograft in combination with adjunctive Imatinib

Entry Criteria

Inclusion Criteria:

1. Patients must have elected to have allogeneic Stem Cell Transplantation
2. Patients under the age of 65 years
3. BCRABL positive CML in first chronic phase
4. Patients with an HLA identical sibling donor or a matched unrelated donor
5. Cardiac ejection fraction >40%
6. Renal EDTA >50 ml/hr
7. DLCO (Diffusing Capacity) >50%
8. Life expectancy > 12 months
9. WHO performance status of 0, 1, 2
10. Patients must be able to swallow capsules
11. Liver Function < 2.5 upper limit of normal
12. All men & women must agree to practise effective contraception during the entire study period.
13. Give written informed consent prior to study specific screening procedures, with the understanding that the patient has the right to withdraw from the study at any time, without prejudice.
14. Be willing and able to comply with the protocol for the duration of the study

Exclusion Criteria:

1. Patients with an allergy to Fludarabine or Imatinib
2. “BCRABL negative” CML
3. Pregnant or lactating women.
4. Patients with organ allografts
5. Patients with any other condition, which in the Investigator’s opinion would not make the patient a good candidate for the clinical trial.

Recruitment number: 30

Treatment plan:
Reduced intensity mini allograft
Commence Imatinib at 300mg on day 35 post transplant
Increase to 400mg after two weeks if this is tolerated
Continue until twelve months or relapse and implement DLI at this time

Points of note:
Patients should be haemodynamically stable before commencing Imatinib

Drug interactions/Concurrent medication:
Patients should not eat Grapefruit or drink grapefruit juice.
The research nurse must be made aware of any new medications the patient is taking.

Side effects:
Patients on Imatinib can experience mild nausea, leg cramps, diarrhoea, facial oedema, fluid retention and bone marrow depression

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