

Targeted Radiotherapy in Reduced Intensity Allogeneic Stem Cell Transplantation

Aim: To assess the role of targeted radiotherapy in allogeneic transplantation in multiple myeloma utilizing reduced intensity conditioning

Background: Reduced intensity conditioning allografts have been shown to be safer, with lower transplant related mortality in comparison to those with conventional high dose conditioning regimens. However, experience with this approach has been disappointing with higher rates of disease progression and relapse. A potential strategy to overcome this problem involves the use of targeted radiation delivered by antibodies to sites of disease.

Method/Design: Phase II study including adult patients with multiple myeloma relapsing post autograft or patients considered to have a high risk of disease progression based on currently accepted parameters (high beta-2 microglobulin and CRP, poor response to at least one line of induction therapy, adverse cytogenetics such as deletion of the long arm of chromosome 13 in metaphases) with an identified HLA matched donor. Exclusion criteria include seropositivity for HIV/ Hep B/C and significant co-morbidities.

Radiolabelled anti-CD66 antibody with Yttrium-90 would be used to direct radiation to the bone marrow prior to transplantation, with the conditioning regimen consisting of fludarabine and melphalan. Multi-colour flow cytometry and molecular techniques would be performed on the marrows of patients for assessment of expression of CD66 on malignant plasma cells.

Evaluation of disease status prior to transplantation would be undertaken to assess the degree of marrow plasmacytosis, serum beta2 microglobulin, serum albumin level and routine biochemistry/haematology parameters. Response to treatment would be assessed and defined according to the EBMT criteria. Assessment of the time to engraftment, chimaerism, presence of acute and chronic graft versus host disease, regimen-related toxicities and infections, as well as event free and overall survival would also be performed.

Statistical analysis of results would involve the use of methods to determine probability of disease free survival, event free survival, overall survival.

Summary: At present, there is very limited data in the literature on the application of this technology in the context of allogeneic SCT. This study would significantly facilitate the understanding of the role of radioimmunotherapy in transplantation, and potentially revolutionize haematopoietic stem cell transplantation by provision of improved treatment intensity without toxicity.