Indolent lymphoma accounts for 35% of all NHL and is associated with a median survival of 9 years. Intensified consolidation with HDT (+/- radiotherapy) and ASCT has been reported to improve progression free survival (PFS)(5, 6) but patients eventually relapse.

MCL accounts for 6% of all non-Hodgkin’s lymphoma (NHL). It is generally considered incurable.

MCL occurs in 50% of all non-Hodgkin's lymphoma (NHL). It is generally considered incurable. Although high response rates can be achieved with initial chemotherapy median survival is only 3-4 years. Intensified consolidation with HDT or radiotherapy and autologous transplantation has been reported to improve progression free survival (PFS), but patients eventually relapse.

Indolent lymphomas accounts for 35% of all NHL and is associated with a median survival of 9 years. Like MCL, it is generally considered to be incurable. PFS also appears to be improved following HDT/ASCT(7).

Against this background, we initiated a pilot study evaluating Id vaccination following high dose therapy and autologous stem cell transplantation for patients with mantle cell lymphoma, indolent NHL, and transformed NHL, to evaluate the feasibility and effectiveness of this post autologous transplantation immunomodulatory strategy.

**Study Objectives**

- To evaluate the ability of Id/KLH to induce immune responses when administered following HDT/ASCT

- To evaluate PFS for patients receiving Id/KLH post ASCT

**Key Eligibility Criteria**

- Follicular Grade 1 or 2 NHL, MCL, transformed NHL, or small lymphocytic lymphoma
- Previous treatment with HDT/ASCT
- Age 18-70
- Previous treated or newly diagnosed
- No prior autologous transplant
- No ongoing steroid treatment
- Meets institutional criteria for HDT/ASCT

**Evaluation of Cellular and Humoral Immune Responses**

To evaluate humoral immune responses, serial dilutions of serum samples are added to wells containing unconjugated patient derived Id or irrelevant Id matched for light chain expression, or KLH. The presence of bound antibody is detected in a standard ELISA using a biotin conjugated polyclonal goat anti-light chain antibody preparation for idiotype detection or a HRP conjugated polyclonal goat anti-human IgG antibody preparation for KLH detection. At any time point, the antibody titer was measured against the patient’s antibody preparation compared with pretreatment levels with no cross reactivity against an unrelated patient’s light chain preparation. Antibody responses to KLH were considered positive if a 16-fold increase in titer was measured compared with pretreatment levels.

For cellular immune responses peripheral blood mononuclear cells (PBMC) are cultured with KLH, autologous Id or a control patient Id and the frequency of CD4+ T cells that stain for cytoplasmic IFN-gamma or TNF-alpha is evaluated. At any time point, a response was considered positive if a minimum two-fold increase in the number of cytoplasmic cytokine-expressing cells was observed over pretreatment levels and, in case of Id-specific responses, without cross-reactivity with control-Id.

**Clinical Responses**

The ability of post-transplant NHL patients who have received a number of prior chemotherapy regimens (including the Hyper-CVAD regimen) to mount Id-specific immune responses suggests that the post-transplant period, during lymphocyte recovery, may be an opportune time to administer Id immunizations. In the setting of minimal residual disease, we have evaluated the induction of an immune response against Id after transplantation. Healthy T cells may be antigen driven and with the vacu "space" for immune reconstitution, we allow a specific post-transplant advantage to the induction of robust Id specific immune responses. This has been demonstrated in murine studies(8) Further studies are needed to determine whether the period of post-transplant T cell recovery may be a window during which tolerance to Id may be overcome.

**Conclusions**

1. Id vaccination following HDT/ASCT is safe and feasible.

2. Id vaccination following HDT/ASCT can induce specific cellular and humoral anti-id responses in both MCL and IL patients who are heavily pre-treated, even following HDT/ASCT.

3. Id vaccination following HDT/ASCT can induce durable remissions even in heavily pre-treated patients with MCL and IL.

**Bibliography**


