

**Randomized Trial of Sirolimus-Based Graft vs.Host Disease Prophylaxis  
after Hematopoietic Stem Cell Transplantation in Relapsed ALL**  
*COG ASCT0431 (PBMTC ONC051)*

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**Synopsis:**

Primary Objective

1. To compare 2-year EFS post transplant in patients undergoing allogeneic HSCT randomized to sirolimus based GVHD prophylaxis versus standard GVHD prophylaxis.

Secondary Objectives

1. Compare rates of relapse, transplant-related mortality (TRM), and acute and chronic GVHD in patients receiving sirolimus-based GVHD prophylaxis vs. standard GVHD prophylaxis.
2. Evaluate the relative contribution of resistance by ALL blasts to cytolytic therapy (chemotherapy/irradiation) as a cause of relapse post transplantation by correlating 1) ALL *in-vivo* blast resistance to sirolimus *in-vivo*, 2) inhibition levels of the mTOR pathway in children treated with sirolimus, and 3) altered resistance pathways in ALL blasts measured by microarray analysis.
3. Evaluate the relative contribution of resistance by ALL blasts to the donor immune response as a cause of relapse post transplantation by correlating the development of donor anti-ALL T-cell response, the development of acute and/or chronic GVHD, and the detection of altered ALL blast immunogenicity after transplant with increasing MRD, persistent recipient chimerism, and relapse.