Title: A Randomized Phase II Trial of Bevacizumab (IND# 7921, Avastin) and Temsirolimus (IND# 61010, Torisel) in Combination with Intravenous Vinorelbine and Cyclophosphamide in Patients with Recurrent/Refractory Rhabdomyosarcoma: A Groupwide Phase II Study (ARST0921)

IRB# 2011-008

Principal Investigator: Carla Golden, MD

Synopsis:
This is a COG Study.

COG conducted a Phase II study (ARST0121) to test risk-based clinical hypotheses in patients experiencing their first relapse or progression of rhabdomyosarcoma (RMS). The overall survival rates observed on ARST0121 were similar to that seen in recurrent patients from IRS-III, -IV pilot, and -IV, suggesting that protocol-driven second-line therapy was no more successful than historic results and that new strategies are necessary to improve the outcome of recurrent RMS.

Inhibition of angiogenesis has resulted in reduced tumor growth in many ex vivo models of pediatric and adult malignancies. This effect has also been independently demonstrated in RMS xenograft tumors.

Temsirolimus is a soluble ester of rapamycin, which is a natural product initially developed as an antifungal drug and then as an immunosuppressive agent with anti-cancer activity. Temsirolimus forms a complex with FK506-binding protein and prohibits the activation of mTOR, similar to sirolimus (rapamycin). Increased mTOR pathway activation has been reported in childhood RMS with an associated decrease in survival. Preclinical data from several research groups suggest that mTOR targeted therapy may be an effective strategy in children with RMS.

The primary goals of this randomized Phase II study are to determine the feasibility of administering bevacizumab or temsirolimus with a chemotherapy regimen of intravenous vinorelbine and cyclophosphamide (VC), and to compare the event-free survival (EFS) between patients with recurrent/refractory RMS treated with VC + bevacizumab and those treated with VC + temsirolimus. The study results will provide background data to support the feasibility of the addition of bevacizumab or temsirolimus to VAC (vincristine, dactinomycin, and cyclophosphamide) chemotherapy in either intermediate- or high-risk RMS patients. In addition, comparison of the EFS between the 2 arms will allow a rational selection of bevacizumab versus temsirolimus as a biologic agent to be tested in patients with newly diagnosed RMS.