

AMERICAN SOCIETY OF CLINICAL ONCOLOGY-ASP JUNIOR CAREER DEVELOPMENT AWARD IN GERIATRIC ONCOLOGY



AWARD RECIPIENT

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PROJECT

"TARGETING TUMOR ANGIOGENESIS IN MANTLE CELL LYMPHOMA"

MENTORSHIP TEAM

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Mantle cell lymphoma (MCL) is a distinct subtype of non-Hodgkin's lymphoma (NHL) characterized by cytoplasmic domains (CD) 5-positive, CD23-negative follicular mantle B cells with typical t(11; 14)(q13;q32) translocation and cyclin D1 protein over-expression. MCL remains incurable and occurs primarily in elderly patients with advanced stage disease. Traditional cytoxan-hydroxyrubicin-ondcovin-prednisone (CHOP)-like chemotherapy produces moderate response with usual time to progression of approximately 1 year. While intensive treatment regimens, including hyper-central venous access device and autologous stem cell transplant, may be associated with more prolonged remissions, treatment-related toxicities can be prohibitive for many elderly patients. Overall, the prognosis for MCL remains poor. Clearly, exploration of novel therapeutics alone or in combination with standard combination chemotherapy, which could offer improved efficacy while preserving quality of life, is a high priority in lymphoma treatment.

My long-term goal is to develop a translational research program in lymphoproliferative diseases, with particular interest in applying low-intensity and novel anti-angiogenic therapeutics in elderly lymphoma patient population in the clinical trial setting. The potential importance of tumor angiogenesis in human lymphoma arises from the association of disease progression with increased angiogenic activity, both in preclinical lymphoma models and clinical correlative studies with archived human lymphoma specimens. In addition, anti-angiogenic therapy, including thalidomide and metronomic oral chemo-regimens, has shown clinical promise in recent pilot studies in selected subtypes including MCL.

The current project is developed based on the hypothesis that disease progression in aggressive MCL is associated with heightened angiogenesis and that targeting vascular endothelial

growth factor pathway in MCL with bevacizumab in combination with chemotherapy will improve progression-free survival while preserving quality of life. The specific aims of this research project are to:

1. Determine the safety profile and clinical efficacy of a novel combination regimen rituximab-bevacizumab-CHOP (RA-CHOP) in a phase II clinical trial for patients with newly-diagnosed mantle cell lymphoma.
2. Characterize the angiogenic profiles (relevant cellular biomarkers of tumor neo-angiogenesis) of MCL patients in prospectively-designed correlative studies during RA-CHOP treatment.

The correlative aspects of the proposed study complement the trial in a translational fashion that can potentially provide important insights into lymphoma biology and facilitate rational design of future therapeutic strategies targeting lymphoma vasculature, both in MCL and in other subtypes.

The American Society of Clinical Oncology-ASP Junior Career Development Award in Geriatric Medicine will provide valuable support for my career development as an independent translational researcher and promote further investigation on novel lymphoma therapeutics including anti-angiogenic therapy in the elderly population. In particular, this award will provide protected research time for the implementation of the proposal as well as educational activities on research methodologies in geriatric oncology through seminars. With the support of this award and the mentorship of Katherine A. Hajjar, MD, Mark S. Lachs, MD, and John P. Leonard, MD, I will have a great opportunity to develop my clinical and translational research focus on the pathogenic mechanism of lymphoma angiogenesis and its potential clinical implication, with the ultimate goal of improving the clinical outcome for elderly lymphoma patients.