October 14, 2010

Positive Immunotherapy Trial Results Published During iSBTc Annual Meeting

Positive clinical trial results from two separate immunotherapy studies were published amidst the excitement of the 2010 iSBTc Annual Meeting, underscoring the rapid, promising growth in the field of cancer immunotherapy.

Anti-GD2 Antibody with GM-CSF, Interleukin-2, and Isotretinoin for Neuroblastoma. Yu, AL. et al. N Engl J Med 2010; 363: 1324-1334

In a multicenter, Phase III randomized trial published September 30, 2010 in the *New England Journal of Medicine*, immunotherapy in combination with standard treatment (isotretinoin) significantly improved survival of high-risk patients with neuroblastoma. Compared to patients treated with isotretinoin alone, treatment with anti-GD2 antibody, GM-CSF and interleukin-2 combined with isotretinoin was associated with significantly improved event-free survival (46.5% vs. 66% at 2 years; $p = 0.01$) and overall survival (75% vs. 86% at 2 years; $p = 0.02$). These encouraging results and implications for other cancer immunotherapies were presented by co-investigator and iSBTc member Paul M. Sondel, MD, PhD, (University of Wisconsin Carbone Cancer Center, Madison, WI) as part of the iSBTc Workshop on Monoclonal Antibodies in Cancer, October 1, 2010. Slides of Dr. Sondel's presentation on this trial will be available on the iSBTc website in the coming weeks.

In Situ Vaccination with a TLR9 Agonist Induces Systemic Lymphoma Regression: A Phase I/II Study. Brody, JD, et al. JCO 2010; 28: 4324-4332

Positive results of a novel early phase clinical trial with intratumoral injection of a Toll-like receptor agonist in combination with radiation in 15 patients with low-grade B-cell lymphoma were published on October 1, 2010 in the *Journal of Clinical Oncology*. The Phase I/II study was directed by Ronald Levy, MD (Stanford University School of Medicine, Stanford, CA), winner of the iSBTc 2006 Richard V. Smalley, MD, Memorial Award. *In situ* treatment with a synthetic oligodeoxynucleotide (CpG), an effective TLR-9 agonist, in combination with low-dose radiotherapy at the same tumor site induced tumor reactive memory $CD8^+$ T cells and positive clinical responses at distant tumor sites that had not been treated. These results indicate that modification of the tumor microenvironment is capable of inducing a systemic, active immune response against the tumor. Of the 15 patients treated with this combined immunotherapeutic approach, one had a complete response, three had partial responses, and two other patients had prolonged stable disease. These data may prompt additional strategies to promote systemic anti-tumor immunity through manipulation of the tumor microenvironment.