

**VCU**

Leaders' Update on Translational Research

Dear colleagues,

Massey Cancer Center has a strong history of translating our basic science research into successful investigator-initiated trials (IITs). We are continuing to develop and conduct promising Massey IITs, and I would like to highlight a couple of recent examples.

An exciting Massey IIT for solid tumors is a phase 2 trial currently open. It is testing the benefits of adding an experimental immunotherapy combination of decitabine and pembrolizumab prior to standard chemotherapy and surgery for breast cancer patients. The trial is being led by Harry Bear, M.D., Ph.D, and is based on his laboratory research, which showed that the addition of decitabine increases the efficacy of immune therapy in mouse models of breast cancer. The study is recruiting patients with locally advanced, HER2-negative breast cancer for whom neoadjuvant chemotherapy is being recommended as standard treatment. The trial is assessing whether decitabine may increase the amount of tumor antigen targeted by a patient's immune response and decrease immune suppression by other white blood cells. Pembrolizumab blocks suppression of T lymphocytes by the cancer and improves the specific ability of lymphocytes to seek out and kill tumor cells. After being treated with immunotherapy, trial participants will then undergo a standard treatment regimen for HER2-negative breast cancers, which includes neoadjuvant chemotherapy for about five months, followed by surgery, if feasible. The trial has an expected duration of three years and is planning to open at Massachusetts General Hospital after the lead-in phase (11 patients enrolled). Roswell Park and UVA are also interested in participating.

An exciting Massey IIT for hematologic malignancies is poised to open later this year. A phase 1 trial led by Danielle Shafer, D.O., it aims to test the safety of a regimen combining the experimental NEDD8-activating enzyme (NAE) inhibitor pevonedistat and the FDA-approved histone deacetylase (HDAC) inhibitor belinostat for the treatment of patients with relapsed/refractory acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The trial is predicated on research conducted in my laboratory and spearheaded by Liang Zhou, M.D., Ph.D., which found that pevonedistat and belinostat interact synergistically by reciprocally disabling the DNA damage response (DDR) in AML/MDS cells. This combined treatment markedly reduced tumor burden and significantly prolonged survival with negligible toxicity in AML xenograft models. The trial is anticipated to open in the fall at Massey and Rutgers Cancer Institute of New Jersey and will be supported by the NCI Experimental Therapeutics Clinical Trials Network (ETCTN), which established partnerships between the pharmaceutical industry, academic institutions and individual investigators for the early clinical evaluation of innovative cancer therapies.

In addition to the trials that I highlighted, multiple other IITs are currently underway, nearing completion, recently published or in development. Please visit the [Massey news blog](#) often for further updates about the cancer center's translational research.

Thank you to all of our Massey researchers whose work helps to advance our IIT program and bring important discoveries from our laboratories into our clinics. I look forward to continuing collaborations between basic and clinical Massey investigators that build on the success of our translational science initiatives.

Regards,

Steven Grant, M.D.

Associate director for translational research and co-leader of the Developmental Therapeutics program