Trial Available for Patients who Recur after HER-2/neu Vaccination

Adoptive immunotherapy has evolved from the preclinical model to a potentially feasible treatment for advanced cancer.

In this trial, we give T cell infusions to cancer patients who have recurred after receiving one of our HER2 vaccines. T cell infusions involve growing patients’ own immune cells (trained to recognize HER2) into millions or billions, and then infusing them back into patients. We have completed the first arm of the study and are now enrolling to the second arm.

Population
- Previously immunized with a TVG HER2-specific vaccine
- Measurable disease that includes extraskeletal metastasis

Treatment
- ONTAK infusion for immune conditioning
- Three T-cell infusions, 10 days apart
- Follow-up visit 20 days after last T-cell infusion

Objectives
- Assess feasibility, safety, immune response, and anti-tumor effects of T cell infusions

Visits
- Five visits total in Seattle

Information
- Please contact Nicole Bates, Research Coordinator, at (206) 543-6620 or nbates@uw.edu

From our Director: A Call to Action for Advancing Research

Dear Friends of the Tumor Vaccine Group,

We at the TVG are fortunate to live our passions every day by working in translational research. Hunched over a lab bench or cell culture flask, sometimes it is easy to forget the real reason our work exists: to help people with cancer. In the same way, as a patient or interested citizen, it can be tough to understand what happens behind laboratory doors. But the fact is that you—America’s taxpayers—fund our grant-supported research, which means that ultimately, we are accountable to you. I believe that everyone has a role in advancing medical science, and I am asking you to help.

You don’t have to quit your day job and become a researcher, and you don’t have to donate your body to science; you can make a difference in research just by sharing your voice. That’s exactly what Patti Bradfield did several years ago. After watching her daughter die from inflammatory breast cancer (IBC), she began calling every doctor and researcher she could find to ask: why aren’t you studying IBC? Her dedication turned into action, and now our group is working to bring an IBC vaccine into clinical trials. I encourage you to do the same thing: find a topic in research you care about, find a researcher working in that field, and then make a phone call.

If you would like to do more than call, researchers nationwide are always looking for patients and healthy volunteers for clinical trials. While many new exciting cancer treatments are being tested in clinical studies, only about 3% of cancer patients ever enroll in a clinical trial. Without these patients’ help, we can never bring new drugs or treatments to market. Researchers also look to patients and healthy volunteers to donate blood—just a one-time blood draw can help us discover new cancer antigens and antibodies that allow us to develop new vaccines and immune therapies.

To all those who have participated in and supported our research: thank you! Medical research is intended to serve you, and to make that happen, researchers in labs and clinics need to hear your input. I encourage you to make your voice heard, support health causes that matter to you, and play an active role in shaping the course of research.

Sincerely,

Mary L. (Nora) Disis, MD
Tumor Vaccine Group Founder & Director

www.tumorvaccinegroup.org 815 Mercer Street, Seattle, WA 98109 866.932.8588
Meet the TVG:

Jennifer Childs, MPH

TVG researchers rely on Ms. Childs to keep their research trials in compliance with a host of agencies and regulations. She also brings her organizational skills to her home life, as a talented cook and gardener!

Jennifer Childs, regulatory coordinator for the TVG, works hard to keep nearly a dozen clinical trials in regulatory compliance at any given time. She is an expert in working with local, statewide, and national agencies to allow us to advance our research and clinical program.

TVG: Most people aren't aware of the work required to keep a clinical trial in regulatory compliance. Which agencies do you work with to keep TVG trials approved and running?

Jennifer: A lot! At the national level, we are accountable to the FDA, National Institutes of Health, and Department of Defense. We also have to maintain regulatory approval from our local Institutional Review Board, Scientific Review Committee, Radiation Safety Committee, and Budgeting and Billing Office. In addition, we have to keep current information about all active clinical trials on the website www.clinicaltrials.gov.

TVG: That sounds like an alphabet soup of regulators. Impressive! What would you say is your biggest challenge in managing all that regulatory work?

Jennifer: I often struggle with the time it takes to make changes to a clinical trial. It's easy to overlook the many steps required, and even small changes can take months to complete. You can't just change a protocol on a whim: it requires planning, multiple regulatory approvals, and final implementation.

TVG: What do you like best about working for the TVG?

Jennifer: We work on the cutting edge, and I love having license to [...] advance our research.

TVG: How about life outside work? What are your hobbies?

Jennifer: Well, I love to cook, and I'm reliving my microbiology past with current experiments in yeast-based breads. I also love to garden. Actually, my husband and I are currently applying to designate our property as a "backyard wildlife sanctuary."

Thanks to Jennifer for her great work and dedication to the TVG's clinical trials program! Truly, we couldn't do our research without her.

Jennifer presents our cancer vaccines at a research conference.

To view these posters or any other posters, abstracts or podcasts from the Symposium go to: www.sabcs.org/EnduringMaterials/Index.asp
The insulin-like growth factor (IGF) pathway is associated with proliferation and survival in cancer. In particular, IGF-binding protein-2 (IGFBP-2) is overexpressed in breast cancer cells. This pre-clinical research study addressed whether IGFBP-2 may be a useful target for the immunomodulation of breast cancer by eliminating IGFBP-2-overexpressing breast cancer cells.

The study first addressed whether IGFBP-2 was immunogenic in breast cancer patients. It was found that sera (parts of blood) from breast cancer patients were more likely to have antibody immunity specific to IGFBP-2 when compared to volunteer donors (Figure 1). It was also shown that the majority of peptides (pieces of protein) from IGFBP-2 can be recognized by human T cells, both in breast cancer patients and volunteer donors without cancer. Additionally, T-cells specific for IGFBP-2 peptides were able to respond to IGFBP-2 protein.

Since human IGFBP-2 protein has very similar structure in mice, IGFBP-2 vaccination was tested in a mouse breast cancer model. The neo-transgenic mice were injected with the IGFBP-2 vaccine followed by inoculation with mouse mammary carcinoma (MMC) cells that express IGFBP-2 protein. The mice mounted a T-cell response when vaccinated with an IGFBP-2 peptide vaccine mix. The IGFBP-2 peptide vaccination inhibited tumor growth by 50% compared to the control groups of mice (Figure 2). In order to show that IGFBP-2 specific T-cells were mediators of tumor cell inhibition, adoptive T-cell therapy was also tested in the mouse model. A single infusion of IGFBP-2-specific T cells inhibitor tumor growth by 60%.

This was the first report of IGFBP-2 as a human tumor antigen that may be a functional therapeutic target in breast cancer. Our group is working in the lab now to develop an IGFBP-2 vaccine!

You can read the entire article here: https://depts.washington.edu/tumorvac/publications.php.
Welcome to our newest TVG researchers!

Megan O’Meara, MD
Dr. O’Meara received her medical degree from the University of Arizona College of Medicine in 2005 and completed her Internal Medicine Residency at the University of Washington. At the TVG, she will bring her extensive research and medical expertise to develop a multi-antigen vaccine that targets proteins involved in breast cancer progression and metastasis.

Lauren Rastetter, BS
Ms. Rastetter worked as an assistant for the UW Harrington Lab as an undergrad, studying prion diseases. She became interested in cancer research through her volunteer work with Relay For Life at UW. She will bring her great organizational and research skills to the TVG to develop a database for the lab and assist our scientists with preclinical experiments.

The Tumor Vaccine Group Team

Principal Investigators
Mary L. (Nora) Disis, MD, Program Founder & Director • Hailing Lu, PhD, Laboratory Investigator
Lupe Salazar, MD, Clinical Investigator • Ron Swensen, MD, Clinical Investigator • Heidi Gray, MD, Research Physician

Administrative Team
Josh Aaseng, Project Assistant • Tess Bayon, Program Assistant • Molly Boettcher, Program Specialist
Kathy Tietje, PhD, Program Manager

Scientific Team
Laleh Bigdeli, MD, Research Assistant • Liz Broussard, MD, Research Scientist • Denise Cecili, PhD, Research Scientist
Yushe Dang, PhD, Research Scientist • Ekram Gad, PhD, Research Scientist • Dan Herendeen, PhD, Research Scientist
Greg Holt, MD, PhD, Senior Fellow • Carol Inatsuka, MS, Research Scientist • Emily Jackson, Research Scientist
Vy Lai, PhD, Research Scientist • Jianing Mao, PhD, Senior Fellow • Megan O’Meara*, MD, Senior Fellow
Chris Neeley, MS, Research Scientist • Lauren Rastetter*, Research Scientist
Meredith Sfota, Research Scientist • Ann Wang*, MA, Research Assistant
Mei Wu, PhD, Research Scientist • Yi Yang, Research Scientist

Clinical Team
Andrew Coveler, MD, Senior Fellow • Nicole Bates, Screening Coordinator
Jennifer Childs, Regulatory Coordinator • Doreen Higgins, Research Nurse
Bhavesh O’Byrne, Data Coordinator • Liz O’Donoghue, Database Developer

Student Assistants
Rachel Kim, UW • Mariam Shehata, UW • Vania Wang, UW

*Please join us in welcoming these new researchers, staff, and volunteers to the TVG!

Current TVG Clinical Trials

Below is a list of the Tumor Vaccine Group studies that are currently enrolling patients. For more information about a study, please call Nicole Bates at 866.932.8588, or visit our website: www.tumorvaccinegroup.org.

<table>
<thead>
<tr>
<th>Short Title of Study</th>
<th>Patient Population</th>
<th>Treatment Information</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adoptive T Cell Therapy</td>
<td>Cancer relapse after receiving a TVG vaccine</td>
<td>One dose of ONTAK and 3 infusions of T cells</td>
<td>I</td>
</tr>
<tr>
<td>Priming with Vaccines Followed by Adoptive T Cell Therapy</td>
<td>Maximally treated HER2+ Stage IV breast cancer</td>
<td>3 weekly vaccines, leukapheresis, single dose of Cytoxan, 3 T cell infusions, then 3 booster vaccines</td>
<td>I/II</td>
</tr>
<tr>
<td>ICD Peptide Vaccine</td>
<td>Stage IIIB, IIIC or IV HER2+ breast cancer</td>
<td>6 monthly vaccines</td>
<td>II</td>
</tr>
<tr>
<td>Abraxane/GM-CSF</td>
<td>Platinum resistant or refractory epithelial ovarian, peritoneal, or fallopian tube cancer</td>
<td>Up to six 4-week cycles: weekly Abraxane, weeks 1-3; daily GM-CSF self-injections, weeks 3-4</td>
<td>II</td>
</tr>
<tr>
<td>Imiquimod/Abraxane</td>
<td>Advanced breast cancer with skin or chest wall metastases, unable to stay in remission</td>
<td>Topical imiquimod and IV Abraxane for up to three 28-day cycles</td>
<td>II</td>
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