UW dermatology sets a new precedent in cancer therapy

By Jon Pry Contributing writer | Posted: Thursday, May 26, 2016 12:00 am

A research team led by the head of UW dermatology, Paul Nghiem, has recently presented positive data from phase-two testing of the drug pembrolizumab and its effects on Merkel cell carcinoma, a highly aggressive and dangerous form of skin cancer.

Merkel cell carcinoma is not like most other forms of cancer. Instead, it is caused by a virus that is asymptomatic on the skin. In order for this virus to become active, a certain set of conditions must occur that researchers are not completely clear about at this time. When these conditions occur, a tumor will form on the location of the skin then spread to the lymph nodes, and eventually tumors will develop throughout the rest of the body.

Pembrolizumab was developed in 2014, and is part of a new method of therapy meant to treat cancer called immunotherapy. It is based on the idea of boosting the immune system by maintaining T cells.

T cells are a type of white blood cell that recognize cancer cells or cells infected with a virus. T cells will attach to the malignant or infected cells, which kill the cells to prevent them from multiplying. This doesn’t work properly when cancer is involved.

A protein called programmed cell death 1, or PD-1, which cancer cells make in abundance, kills T cells. The infected cells are then left to multiply and form tumors.

Immunotherapy attempts to prevent this from occurring by using drugs that inhibit PD-1. By doing this, the T cells are free to multiply and fight off the infected cells. This idea was first presented as a viable option in “Safety, Activity, and Immune Correlates of Anti–PD-1 Antibody in Cancer,” by Suzanne Topalian in 2012.

This process is being tested on many forms of cancer, and Nghiem’s work has been revolutionary. His article, “PD-1 Blockade with Pembrolizumab in Advanced Merkel-Cell Carcinoma” was published in The New England Journal of Medicine on April 19, 2016.

The phase-two testing currently in place has yielded results that have never been seen before in Merkel cell carcinoma patients. Virus positive patients, meaning that the patients already have antibodies because the virus was asymptotically present on the skin of the individual before the cancer develops, had a 62 percent response rate to pembrolizumab and a plateau on the number of tumors present in the patients. Virus negative patients, meaning patients without the virus prior to activation and therefore no antibodies, had a
44 percent response rate with a similar plateau. Virus negative patients also develop the first tumor directly in the lymph node, rather than on the skin.

This information is exciting to patients with Merkel cell carcinoma, particularly because the disease is so rare it is understudied and underfunded, said Jamil Qazi, an undergraduate research assistant in Nghiem’s lab.

“People still have it though and the idea that there is something being offered is very exciting and uplifting,” Qazi said.

Merkel cell carcinoma has only about 2,000 new cases every year. Only 50 percent of patients with Merkel cell carcinoma respond to traditional chemotherapy. Even if that does work, the cancer will recur three months later, said Hannah Thomas, another undergraduate research assistant in Nghiem’s lab.

Pembrolizumab has a longer lasting effect on Merkel cell carcinoma and will hopefully get the Food and Drug Administration’s (FDA) approval. If it does, it will be the first FDA approved drug for Merkel cell carcinoma.

The development of pembrolizumab is beneficial to those with Merkel cell carcinoma specifically, but it also presents a unique chance to change how cancer therapy in general is understood.

“Collectively, there are many people, myself included, that believe that this new class of drug, is the single most important cancer therapy ever developed,” Nghiem said in an email. “There is also excitement about the prospects of combining PD1-targeted immune therapy with traditional therapies, such as radiation, as well as with other immune stimulating approaches.”

Knowing that drugs such as pembrolizumab work on Merkel cell carcinoma helps create a whole new avenue of inquiry.

“Going forward, the questions being asked becomes “Why is there such a high response rate and how will we be able to improve the therapy for other cancers?”” said Mac Cheever, a UW professor of oncology and director of the Cancer Immunotherapy Trials Network.

The conclusion drawn from this study is that immunotherapy can work on all sorts of cancers. It also presents a huge commercial opportunity for drug companies to create more effective drugs in the future.

“The Nghiem study was remarkable because we didn’t know if it would work,” Cheever said. “It did more than that, it immediately changed the therapy of choice for Merkel cell cancer.”

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