

December 2016

Dear Friends of Merkel cell carcinoma Research,

### Your Impact

This year has brought exciting milestones in Merkel cell carcinoma (MCC) research and clinical care. As we enter the season of celebrations and appreciation, all of us here at UW Medicine want to express our gratefulness for your generosity to UW Medicine and the Merkel cell carcinoma program. Our progress report below brings you the latest in MCC research and treatment, all of which were made feasible through your generosity.

### 11<sup>th</sup> Annual Merkel Cell Carcinoma Dinner Meeting

Many of you were able to join us on September 12<sup>th</sup> in Seattle for our 11<sup>th</sup> annual Merkel cell carcinoma Dinner Meeting. We hosted 260 patients, family members, clinicians, scientists, and trainees from across the United States. Attendees enjoyed a lovely buffet dinner, music, lab tours and a presentation on the status of research and clinical trials in this cancer, sponsored by generous patients and donors. Highlights of the evening can be found by visiting our newly redesigned [www.merkelcell.org](http://www.merkelcell.org).

### Immunotherapy

As many of you know, there is no FDA-approved therapy for MCC, but we're hoping to change that soon. The Merkel cell carcinoma clinical trials that we are conducting have already begun to change the way this cancer is treated. While there are several therapies that can stimulate the immune system, the most promising emerging option includes a class of drugs called the immune checkpoint inhibitors. Immune checkpoint inhibitors (ICIs) are therapies that turn on the immune system by blocking an inhibitor (a "checkpoint") that normally restrains the immune system. Such agents can sometimes cause the immune system to recognize and destroy a cancer. Tumor cells escape the immune system by pressing "brakes" (like the PD-1 protein) on the surface of killer immune cells. The ICIs block these brakes from getting pressed and allow immune cells to function better. There are several ICIs currently being investigated in MCC, which we detail below.

Pembrolizumab, a type of ICI, was administered as an intravenous infusion every three weeks in the outpatient clinic to 26 patients with metastatic MCC who had not received any prior systemic therapy (no prior chemo therapy). Of those patients, 56% had impressive shrinkage of their tumors. Patients with both virus-positive and virus-negative tumors responded to the treatment. Additionally, 86% of those who initially responded had persistent responses lasting over a year. Such responses are strikingly more long-lasting than are typical of chemotherapy responses. These results, led by our team, were reported in the New England Journal of Medicine this summer.

Avelumab, another ICI that also blocks the PD-1 pathway (it binds to the binding partner of PD-1 called PD-L1), has also shown considerable promise in fighting MCC. This drug was tested in 88 patients with metastatic MCC. These were patients with especially difficult to treat tumors – their tumors had returned after previously being treated with chemotherapy. Of the 88 patients treated, 28 (32%) responded with significant tumor shrinkage that appeared to be extraordinarily more resilient than chemotherapy responses. Over 80% of patients who initially responded to avelumab have impressively durable responses continuing beyond a year. This study was reported in Lancet Oncology in September.

Other ICIs, including nivolumab and ipilimumab, are also in clinical trials for those with advanced MCC. In addition, there are several other immunotherapy approaches being investigated for MCC in clinical trials, including intra-tumoral injection approaches and infusion of immune cells (T-cells or Natural Killer cells). Initial results suggest a promising future for immunotherapies in the treatment of MCC.

The progress we are making in our efforts to better understand and treat skin cancers are further described in some of the publications and articles that are listed at the end of this report. I hope you can take some time to look up the publications on the internet and that give a sense of the important work we are leading. I invite you to share in the pride our caregivers and researchers feel at these accomplishments. Your generosity has helped to make them possible.

## Recognition and Awards

In winter of 2015, I was honored to be named one of Newsweek's Top Cancer Doctors of the year based on nominations from peers around the country.

I also had the opportunity to be the keynote speaker at the 6th Annual Harley Haynes Lectureship and Symposium at Harvard Medical School in March of 2016, with a lecture entitled: "Merkel cell carcinoma: From a book chapter to clinical trials - 15 exciting years thanks to Harley." Dr. Haynes had an enormous influence on my career in terms of becoming a dermatologist and focusing on Merkel cell carcinoma.

## The Year Ahead

The entire Merkel cell carcinoma team is moving forward in each of the areas described above, and I am confident that this trend will continue. We recently also had a great addition to our team, Masaoki Kawasumi, MD, PhD. Dr. Kawasumi, a recipient of the Dermatology Foundation Career Development Award, has an extensive research background in UV skin carcinogenesis and skin cancer prevention. He will be leading an NIH R01 grant research project with me.

An important goal for 2017 is to prepare and submit a very major (\$15 million) NIH grant called a "Program Project Grant." This grant, if funded, will bring together about two dozen scientists from UW and Fred Hutchinson Cancer Research Center to use the immune system to fight MCC. Currently, ICI agents can help about half of patients with MCC and the goals of this grant would be to markedly improve the odds for patients that do not benefit from ICI therapy.

## Thank You

Because of the funding and support received for our work in Merkel cell carcinoma, I am able to carry out my dream work of doing scientific and clinical work that changes how we treat patients. I am particularly excited that I can use these funds to support innovative and novel treatments for patients who currently have no FDA approved options. Your generosity has improved the lives of many patients, families, physicians, and scientists, and, on their behalf and my own, I thank you.

Please consider [making a donation](#) to our Merkel cell carcinoma effort and know that 100% of donations go directly to our MCC research and educational efforts and are fully tax deductible. For now, please know how grateful my colleagues and I are for your support.



**Paul Nghiem, M.D., Ph.D.**  
George F. Odland Endowed Chair in Dermatology  
Professor and Head, Division of Dermatology  
Adjunct Professor, Department of Pathology &  
Department of Oral Health Sciences

## Press, Publications, & Awards

New England Journal of Medicine Original Article:

New England Journal of Medicine "PD-1 Blockade with Pembrolizumab in Advanced Merkel-Cell Carcinoma"  
([http://www.nejm.org/doi/full/10.1056/NEJMoa1603702?query=featured\\_home](http://www.nejm.org/doi/full/10.1056/NEJMoa1603702?query=featured_home) )

News stories on immune therapy for MCC:

Washington Post (Page A1) story by Laurie McGinley titled "The list of cancers that can be treated by immunotherapy keeps growing" (<https://www.washingtonpost.com/news/to-your-health/wp/2016/04/19/breakthrough-cancer-therapy-shows-growing-promise/> )

The Atlantic story by Vann R. Newkirk II titled "Cancer: The Final Frontier"

(<http://www.theatlantic.com/politics/archive/2016/04/cancer-the-final-frontier/478962/> )

Fred Hutch Cancer Research Center story by Susan Keown titled "Finally showing hope: Immunotherapy trial results transforming care for rare skin cancer" (<https://www.fredhutch.org/en/news/center-news/2016/04/pembrolizumab-merkel-cell-carcinoma.html> )

Medscape story by Zosia Chustecka titled "Remarkable Responses in Rare Merkel-Cell Skin Cancer"

(<http://www.merkelcell.org/documents/MedscapeArticle.pdf> )

UW Medicine article "Immunotherapy: Hope for Merkel cell carcinoma patients"

(<https://medicine.uw.edu/news/immunotherapy-hope-merkel-cell-carcinoma-patients> )

AACR article "Pembrolizumab Yields Lasting Merkel-Cell Carcinoma Responses"

(<http://www.merkelcell.org/documents/AACRArticle.pdf> )

Johns Hopkins article "Immunotherapy drug shrinks tumors in half of patients with rare, virus-linked skin cancer"

(<http://www.merkelcell.org/documents/HopkinsArticle.pdf> )

Lancet Oncology story by Holly Baker "PD1 inhibition in advanced Merkel-cell carcinoma"

(<http://www.merkelcell.org/documents/Lancet%20article.pdf> )

MDLinx Interview "Why did you conduct this study?" (<https://www.dropbox.com/s/hpbg81j1lr7l2u5/13-Nghiem.mp4?dl=0> )

An 88 patient clinical trial of Avelumab in patients who had previously received chemotherapy for metastatic Merkel cell carcinoma

(<https://merkelcell.org/news-and-publications/2016/avelumab-in-patients-with-chemotherapy-refractory-metastatic-merkel-cell-carcinoma-a-multicentre-single-group-open-label-phase-2-trial/>)

An editorial that concludes that ICIs are the new standard of care for advanced Merkel cell carcinoma

(<https://merkelcell.org/news-and-publications/2016/checkpoint-inhibitors/>)