



# A PATIENT PARTNERSHIP IN CARE AND RESEARCH

For the past 16 years, Dick Metz has experienced the ups and downs of a cancer diagnosis. He has had clean scans and bad scans, and has experienced joys and disappointments of therapy results, but he has never faltered.

Mr. Metz's journey illustrates the incredible strides that have been made in treating melanoma, a cancer that just ten years ago had a much more frightening prognosis. Making matters more difficult for Mr. Metz was his cancer's tendency to spread to the brain, and the fact that historically patients with brain metastases were completely excluded from clinical trials. Although older therapies resulted in responses in up to 15 percent of patients, the use of contemporary immunotherapy has changed the way oncologists now treat melanoma.

Mr. Metz's chronicle began in 2003 when his dermatologist biopsied a mole on his back and discovered stage II melanoma. Mr. Metz was referred to surgeon, Stephan Ariyan, MD, MBA, where he underwent wide excision surgery, which removes the tumor and a margin of assumed healthy tissue around it. In addition, nearby lymph nodes were checked and a biopsy was taken of the sentinel lymph node, the lymph node that drains the tumor. For Mr. Metz, all lymph nodes were found to be clear and he finally felt that he could exhale. He was then referred to Harriet Kluger, MD, Professor of Medicine (Medical Oncology), to be monitored.

"I felt like I had dodged the bullet," recalled Mr. Metz. "The doctors had me check in with them each year to make sure nothing had spread to other organs in my body. All was fine until a few years later when I started waking up in the middle of the night due to night sweats."

Mr. Metz's primary doctor sent him for an ultrasound, which revealed an 11-centimeter tumor on his liver, later determined to be a metastasis from the melanoma on his back. "I was shocked and surprised that the melanoma cells had escaped into the bloodstream and gone from my back to my liver years later," Mr. Metz said.

"Dr. Kluger explained that if we did not do anything, I only had a matter of months to live. This news sent me into a tailspin. I came out of it in what I call my fight mode. I wanted to become an expert in my disease. I immediately went on the internet to find out any information I could. I wanted to really understand my options and what possible treatments could beat this disease."

The choices of treatment for stage IV melanoma in 2008 were very limited, either chemotherapy—which had limited success, or a form of immunotherapy, high-dose interleukin-2, which required two five-day hospital stays, with one week off in between, followed by scans to see the results of the treatment. Mr. Metz chose to proceed with the interleukin-2, but after completing the treatment, his scans did not show any changes in the tumor.

Dr. Kluger recommended that Mr. Metz visit the National Cancer Institute (NCI) in Bethesda, Maryland for an investigational treatment where he would be considered for a clinical trial for tumor infiltrating lymphocyte therapy (TIL), which activates immune cells to recognize and attack cancer cells. This modality was not available at the time at Yale, but it is now.

Unfortunately, Mr. Metz's blood test revealed high liver enzyme levels from the tumor in his liver, which indicated he was not a candidate for the TIL investigational trial. Instead, the doctors at the NCI recommended surgery to remove as much of the tumor on his liver as possible. They also explained that there was a small chance (15-20 percent) he would not survive the surgery. Considering his chances of survival without surgery were 2-3 months, it was an easy decision. "The liver is one organ that can actually grow back," explained Mr. Metz. "The doctors thought that taking out the tumor would allow the liver to recover, and with normal liver enzyme levels, I might be able to enter the TIL study."

Following the surgery, Mr. Metz continued to return to Bethesda periodically for the next three years for scans and checkups. "All

was well," said Mr. Metz, "until a scan showed that the melanoma had metastasized to my brain. I was devastated because I had been thinking that if something happened, the TIL treatment would be my savior. And now, brain mets (metastases) would preclude me from getting that treatment."

Mr. Metz called Dr. Kluger, who explained the available options and introduced him to Veronica Chiang, MD, FAANS, Professor of Neurosurgery, in March 2011. After further consultation, Dr. Chiang recommended he be scheduled for a Gamma Knife procedure. The Gamma Knife treatment allows a team of radiation therapists and neurosurgeons to give high doses of radiation to a very targeted area of the brain. "After the treatment, my life pretty much went back to normal again."

It was at this time that Mr. Metz wanted to make a difference. He launched The Brain Metastasis Fund to raise money and support Yale Cancer Center's research efforts. "My doctors had been great to me and I wanted to give back. I relied on my former experience working in the insurance and financial industries to begin this initiative. I invited 100 people to a party in my backyard. Seventy-five showed up and we started raising money. To date, we have raised over \$700,000 from private donations," said Mr. Metz.

In fact, one of the major research initiatives resulting from The Brain Metastasis Fund was to support Yale Cancer Center initiated clinical trials that provide access to promising drugs prior to their approval by the FDA. One such class of immunotherapy was looking highly promising at the time, but patients with brain metastases were traditionally excluded from those trials. Therefore, the team at Yale used the funding to initiate the first study of pembrolizumab for patients with brain metastases from melanoma or lung cancer. In 2014, Mr. Metz was accepted into the clinical trial.

After starting on pembrolizumab, which at the time was a much higher dose of the drug than what is used today, no brain metastases developed. However, Mr. Metz could not tolerate the higher dosage and he was taken off the trial and instead placed on the FDA-approved dosage of pembrolizumab, which allowed stabilization of the disease and for Mr. Metz to recover functionally to where he is today.

"I have the highest regard for Dr. Kluger. She is incredibly smart and talented. And she's never given up on me. She continues to find new ways to keep me going. Today, I'm still on pembrolizumab along with phenobarbital to lessen the side effects. If it wasn't for her and her team, I would not be alive today."

Mr. Metz cherishes the encouragement and assistance that his wife of 46 years, his two sons, and his grandchildren have given him. "They continue to be my greatest joy. I treasure the time I spend with my family. My cancer has changed my perspective and my life. I have looked at myself and set new priorities. I am fortunate to be surrounded by good doctors, a wonderful family, and many friends. I know that there is a tremendous amount of work being done in the research field. That gives me hope that someday I will be totally healed." ☺



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