

# The Brain Stem

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December 2019



## FDA Approves Immunotherapy Drug for Brain Tumors

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For the first time in history, the FDA has approved a drug based solely on the presence of a genetic mutation (high microsatellite instability, MSI), without limitations on the cancer site or specific cancer type it can be used to treat. The drug is called pembrolizumab.

This landmark approval means a patient with pancreatic cancer and a patient with brain cancer may share the same genetic profile and benefit from the same treatment. This milestone represents a new strategy to expedite cancer therapy approval in an era of medical research driven by genetic markers and precision medicine. It is especially good news for brain cancer patients who need new treatment options.

When people are diagnosed with cancer, treatment options vary depending on the type, grade and location of their cancer.

Those options include medications (immunotherapy, chemotherapy, targeted therapy, etc.), radiation therapy and surgery. Immunotherapy is a certain type of cancer treatment that “boosts” a person’s own immune system, giving it greater cancer-fighting potential. It increases the ability of certain immune system cells to recognize and destroy cells that exhibit abnormal growth, like cancer cells.<sup>1</sup> Chemotherapy, is different: It targets rapidly dividing cells – a classic characteristic of cancer. Chemotherapy drugs tend to affect other non-cancer cells that also divide rapidly, such as cells of the skin, gut lining and liver; hence, chemotherapy often has side effects.<sup>2</sup>

Pembrolizumab is one of many immunotherapy treatments against cancer. This drug works by specifically targeting the programmed cell death 1 (PD-1) receptor of

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lymphocytes – the white blood cells that protect our bodies against bacteria, viruses and abnormally behaving cells, such as cancer.<sup>3</sup> In normal conditions, PD-1 works in our favor to prevent our immune system from attacking our own cells, tissues and organs. But certain types of cancers have developed a mechanism to activate the PD-1 pathway in lymphocytes and “hide” from immune cells by pretending to be “normal” cells.

Pembrolizumab was first approved in 2014 for treating people with metastatic melanoma, a very aggressive cancer, after a clinical trial showed it helped shrink tumor size, reduce the risk of disease progression and, ultimately, prolong patient’s lives.<sup>4</sup> Due to these unprecedented positive results for a such an aggressive cancer type, another trial called KEYNOTE-001 trial 5 was developed in hopes of expediting FDA approval of immunotherapies for treating other aggressive cancer types – such as lung, pancreas and brain tumors. KEYNOTE-001 trial 5 included people

with cancers from different body parts; however, all shared a similar genetic abnormality known to make their cancers more susceptible to immunotherapy. This study was only possible due to a unique design used here – called a basket trial. A major advantage of a basket design compared to a classical trial design is the ability to use fewer patients over a shorter period of time to discover the effectiveness of a new therapy.<sup>6</sup>

We can now consider pembrolizumab for people with tumors that can’t be treated with surgery or those with metastatic solid tumors expressing high microsatellite instability (MSI). MSI is a change that is often found in the cancer cell DNA.<sup>7</sup>

As with any cancer treatment, patients are curious about potential adverse events. Fortunately, immunotherapy seems much less toxic than conventional chemotherapy, and only the minority of patients develop severe or life-threatening side effects, such as cardiovascular events or bone marrow

suppression. Because pembrolizumab acts as a pro-inflammatory agent, side effects include inflammation of the skin, lung and GI tract.<sup>8</sup>

In February 2019, researchers analyzed the effects of pembrolizumab in patients with recurrent glioblastoma multiforme (GBM), the most common – and most aggressive – type of brain cancer.<sup>9</sup> Their study revealed that when given to patients before surgery, pembrolizumab nearly doubled GBM patients’ survival.<sup>9</sup> It also showed that pembrolizumab increased lymphocyte production which helped kill cancer cells.

Immunotherapy is an innovative, groundbreaking cancer treatment that has led to many encouraging results. With the drug’s early approval, it has altered the way in which we can develop new cancer therapies.

As always, talk with your doctor about the different treatment options and clinical trials available for your condition. ■

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## The NIMBLE App: A New Way to Guide Treatment for Patients With Brain Metastases

Joseph Bovi, MD, Radiation Oncologist

**A**mong tumors that arise within the skull, brain metastases are the most commonly diagnosed. More than 200,000 patients will be diagnosed this year alone, and the incidence is on the rise. (Brain metastases are tumors that started elsewhere in the body and spread to the brain; whereas, a primary brain tumor starts in the brain.) People with brain metastases have unique needs requiring complex medical decision-making, and they have diverse prognoses. Currently, patients with brain metastases are discussed within the framework of our Brain and Spine Tumor Program’s tumor board, which meets every

Wednesday morning to review each person’s case and together, come up with an appropriate, evidence-based treatment plan. The tumor board includes specialists from neuro-oncology, neurosurgery, radiation oncology, neuro-pathology, neuro-radiology and neuro-psychology. It’s not unusual for patients to present to the hospital with a brain metastasis and wait several days to a week until the next brain tumor board discussion. This path can cause delays in patient care and, at times, prolonged hospital stays.



Joseph Bovi, MD

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# Advanced Therapies for Treating People With Brain Metastases

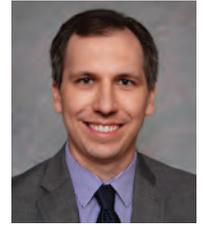
Jonathan Thompson, MD, Medical Oncologist

Treating brain metastases poses multiple challenges. Patients' neurologic symptoms can be debilitating, and recovery can be slow. Historically, medical therapies for cancer, such as chemotherapy, have not been able to penetrate the brain very well and haven't always reliably controlled brain metastases. Radiation therapy can control brain metastases. However, older techniques like whole brain radiation can lead to significant side effects like fatigue, balance and memory issues. Leksell Gamma Knife® is a newer radiation technique that targets the radiation dose to specific cancer spots and spares normal, healthy brain tissue. It is also easier to tolerate. Fortunately, along with improved radiation therapy techniques, newer medical therapies show significant promise in treating brain metastases.

Targeted therapies are medications (usually pills) that shut down mutated or abnormal proteins that cause cancer growth. While patients have cancer mutations we can target such as EGFR, ALK, ROS-1, oral targeted therapies shrink cancer much better and result in much longer remission than chemotherapy. Targeted therapies also tend to have fewer side effects than chemotherapy. Importantly, many of the newer targeted therapies have an excellent ability to penetrate the brain and shrink brain metastases. When metastatic brain tumors have a mutation we can target, using targeted therapies may allow the patient to delay brain radiation therapy or avoid it altogether.

I focus on treating patients with lung cancer. They have a 25-30% chance of having a targetable mutation, and testing for tumor mutations at cancer diagnosis is a standard part of our practice. Many other cancers, including melanoma and

gastrointestinal cancers, also have targetable mutations. At diagnosis, we encourage our patients to ask their oncologist about cancer mutation testing and targeted therapies as options to treat their cancer.



Jonathan Thompson, MD

When patients do not have targetable cancer mutations, immunotherapy may be an option. Immunotherapy is the newest and most promising wave of cancer therapy. These medications cause the immune system to act as a weapon against cancer cells. If effective, immunotherapy controls cancer much longer than traditional chemotherapy. The immune system can create a "memory" against cancer cells and control cancer for years for some patients. Early studies show that immunotherapy can also shrink brain metastases and for some patients, immunotherapy can be considered as the first option for treating their brain metastases. While immunotherapy doesn't work for everyone, we can sometimes identify markers that can signal the probability of immunotherapy working. It is important for patients to ask their oncologists about immunotherapy for their cancer care.

Overall, there is reason for optimism for patients facing brain metastases. Radiation, surgical and medical therapies are constantly improving and can offer long-term control of cancer for more and more people. Patients should be sure to ask their oncology teams about each of these options for treating brain metastases and should consider clinical trials if standard options are not adequate. ■

## NIMBLE continued

To resolve this issue, our program designed a mobile app based on the complicated protocols involved in treating brain metastases. We call it NIMBLE, which stands for Network for the Integrated Management of Brain Metastases: Linking Experts. It has three components. One is an educational tool for inpatient and outpatient providers to understand a comprehensive, data-driven algorithm for brain metastases management. The app also provides a mechanism by which



providers can submit a patient for consideration of 'virtual tumor board' discussion, which is encrypted to safeguard patient privacy. Finally, the app creates a virtual tumor board that allows providers to communicate in real time to generate a consensus opinion that guides the best possible management of the patient in question.

More important than the app is the formation of a dedicated Brain Metastasis Program – a vital complement to our existing Brain and Spine Tumor Program, which treats

people with primary brain tumors. (Primary means the tumor started in the brain.) For the first time, we will have a dedicated service to include all specialties critical to the inpatient and outpatient management of our patients with brain metastases.

Our goal is to create timely, evidence-based treatment plans while reducing the length of hospital stays and delays in care. We plan to pilot the Brain Metastasis Program and app in early 2020. ■



## Support Groups and Events

The Froedtert & the Medical College of Wisconsin Cancer Network offers support groups and sponsors events of interest to brain tumor patients and their families. For more information about our support groups, please visit [froedtert.com](http://froedtert.com), or call **414-805-3666** or **800-272-3666** (unless otherwise noted).

### BRAIN AND SPINE TUMOR SUPPORT GROUP

The Brain and Spine Tumor support group is for patients and family members looking for information and encouragement. Meetings are designed for open discussion of concerns related to brain and spine tumors with many sessions featuring speakers who focus on a variety of topics specific to these diseases.

Meets monthly on the third Tuesday of each month. Times vary.

Froedtert & MCW Clinical Cancer Center at Froedtert Hospital campus.

For information, please see the listing in the Hope Clinic at the Clinical Cancer Center, or call **414-805-3666** or **800-272-3666**.

### YOUNG ADULT ONCOLOGY GROUP

Children's Wisconsin offers the Young Adult Oncology Group for cancer survivors (on and off treatment) ages 18 to 39. This group provides survivorship support, education and social activities.

Meets monthly. Dates and times vary.

Sponsored by Children's Wisconsin, the Medical College of Wisconsin and the Clinical Cancer Center.

More information: Kristin Bingen, **414-955-4148** or [aya@mcw.edu](mailto:aya@mcw.edu).

### JOURNEY TO WELLNESS CANCER SUPPORT GROUP

This support group's open forum provides the chance for all cancer patients wherever they are in their journey to share information and experiences and receive encouragement and education. Topics vary. Adult family members, significant others and caregivers are also welcome to attend.

Cancer Care Center at Froedtert Menomonee Falls Hospital campus  
Treiber Conference Rooms 4 and 5  
Fourth Monday of month; January, March, May, July, September, November; 6:30-8 p.m.

Moorland Reserve Health Center  
Garden Level Conference Room  
(Take elevator down to Garden Level.)

Second Monday of each month, 5:30-7 p.m. (No meeting in July.)

Offered through the Froedtert & MCW Cancer Network: Kettle Moraine YMCA, West Bend, First Wednesday of month; February, April, June, October, December; 6-7:30 p.m. (No meeting in August.)

For more information, call **414-805-3666** or **800-272-3666**.

### CANCER CAREGIVERS SUPPORT GROUP

This support group is for friends, family members or others caring for people with cancer. It promotes open communication of feelings, as well as providing relaxation and stress relief. Various topics of interest to the caregiver are also presented. This group is made possible by donations to Froedtert Hospital Foundation.

Meets monthly on the fourth Tuesday of each month. (No meeting in December.) 5:30-7 p.m.

Clinical Cancer Center  
Conference Room J, Lobby Level  
Various speakers are offered.

For more information, call **414-805-3666** or **800-272-3666**.

### EPILEPSY SUPPORT GROUP

This support group is open to people with epilepsy, their family members and caregivers. Each month, a guest speaks on topics related to seizures.

Meets monthly on the fourth Wednesday of each month. (No meeting in November or December.) 6:30-8 p.m.

Froedtert Hospital  
2NT Conference Room  
North Tower, Second Floor

For questions, concerns or suggestions, please call Linda Allen, RN, Epilepsy Program coordinator, at **414-805-3641** or LeeAnn Lathrop, MSW, social worker, at **414-805-2894**.

## PLEASE JOIN US ON SOCIAL MEDIA

A Facebook page has been created to share information and provide opportunities to connect with and learn from others affected by a brain or spine tumor. You'll find information about events, meetings and classes and the latest research and treatments. If you are interested, follow the page at:

[facebook.com/MCWBrainSpine/](https://www.facebook.com/MCWBrainSpine/)

You can also follow our group on Twitter: [@MCWBrain\\_Spine](https://twitter.com/MCWBrain_Spine)