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F.D.A. Allows First Use of a Novel Cancer Drug

By ANDREW POLLACK SEPT. 4, 2014

The Food and Drug Administration on Thursday approved the first of an eagerly awaited new class of cancer drugs that unleashes the body's immune system to fight tumors.

The drug, which Merck will sell under the name Keytruda, was approved for patients with advanced melanoma who have exhausted other therapies.

Cancer researchers have been almost giddy in the last couple of years about the potential of drugs like Keytruda, which seem to solve a century-old mystery of how cancerous cells manage to evade the body's immune system.

The answer is that tumors activate brakes on the immune system, preventing it from attacking them. Keytruda is the first drug approved that inhibits the action of one of those brakes, a protein known as PD-1, or programmed death receptor 1.

"This is really opening up a whole new avenue of effective therapies previously not available," said Dr. Louis M. Weiner, director of the Georgetown Lombardi Comprehensive Cancer Center in Washington and a spokesman for the American Association for Cancer Research. "It allows us to see a time when we can treat many dreaded cancers without resorting to cytotoxic chemotherapy."

This general approach might work for many types of cancer, though so far the main successes in clinical trials have come against the deadly skin cancer melanoma, lung cancer and kidney cancer.

But the treatments will not be inexpensive. Merck said Thursday that the drug, known generically as pembrolizumab, would cost about $12,500 a month, or about $150,000 a year.

Merck said the price was in line with that of other cancer drugs, though it seemed to be a bit higher than some. Many cancer doctors have already complained about the rapidly escalating prices of cancer drugs, which they said could put treatments out of reach for some patients.

Merck has won a race to market in the United States against Bristol-Myers Squibb, Roche and AstraZeneca, which are in advanced stages of testing drugs that block the action of PD-1. Bristol's drug, nivolumab, being developed with Ono Pharmaceutical, was approved two months ago in Japan, also as a treatment for advanced melanoma.

Some Wall Street analysts have said that collectively cancer immunotherapy drugs could achieve annual sales of tens of billions of dollars.

Keytruda was given accelerated approval by the F.D.A., allowing it to reach the market without the three typical phases of clinical trials needed to show a drug can prolong lives.

Keytruda was approved based on what was essentially an extra-large Phase 1 trial involving 173 participants who all received the drug, with no control group. Tumors shrank in about 24 percent of patients, the F.D.A. said, with the effect lasting at least 1.4 to 8.5 months and continuing beyond this period in most patients.

"Even the very preliminary results on a handful of patients, 20 or so, indicated a high degree of activity," Dr. Richard Pazdur, who oversees cancer drugs at the F.D.A., said in an interview Thursday.

Merck will now have to conduct two controlled clinical trials to verify that the drug can prolong lives and delay the progression of disease.

Robert Waag, a professor of electrical engineering at the University of Rochester, had a series of operations and drugs to fight melanoma lesions, but the cancer kept spreading.

"I watched the metastases spread and grow," he said. "I figured I was

a goner, I could tell you that."

Mr. Waag, 75, entered a clinical trial for pembrolizumab at the University of Pennsylvania, near his second home, in Ocean City, N.J.

"The PD-1 agent went after it and really did a job," he said. He said his latest scan showed no evidence of metastatic disease. He said the drug caused no side effects.

Keytruda, which is a type of protein called a monoclonal antibody, is the sixth new melanoma drug approved since 2011, transforming care of a disease that, once it had spread, usually meant a quick death.

One of those new drugs, Bristol-Myers' Yervoy, or ipilimumab, was actually the first immunotherapy approved for melanoma. It blocks a different brake on the immune system, known as CTLA-4.

Keytruda, which is given by infusion every three weeks, is approved for now only for patients who have first tried Yervoy. Patients also have to first try pills known as BRAF inhibitors if they are eligible for those drugs.

Dr. Antoni Ribas, a melanoma specialist at the University of California, Los Angeles, said that patients who failed to respond to both Yervoy and BRAF inhibitors would probably survive only a few months.

But in a clinical trial of Keytruda that he helped conduct, 69 percent of patients were alive after one year, including 65 percent of those who had tried Yervoy.

"It's away from any chart that we could think of," he said.

Inhibitors of PD-1, researchers say, activate an immune response more specific to the tumor than Yervoy does, which reduces the risk of side effects. Keytruda's label warns that it can cause immune system reactions that can damage the lungs, colon, liver, kidney and other organs. However, that warning is not inside a black box, the strongest level of caution.

Melanoma was known in the past to be susceptible to being subdued by the immune system. So it is not surprising that the immunotherapy drugs have first been approved for that disease.

About 76,000 Americans will get melanoma this year and 9,700 will die from it, according to the F.D.A. Experts say a major cause of the

disease is exposure to the sun.

But researchers say it is somewhat surprising that the PD-1 drugs also seem to show signs of working for some patients with lung cancer. There are also preliminary signs of effectiveness against bladder, gastric and some other types of cancer.

Dr. Roger M. Perlmutter, head of research and development at Merck, said the company was testing Keytruda in about 6,000 patients with 30 different tumor types. “It’s almost a daily event that we initiate new trials,” he said.

Companies are also teaming up with one another to test combinations of immunotherapy drugs, since a single drug will not work for all patients.

Dr. Weiner of Georgetown, an expert on immunotherapy, said that by unraveling the secrets of cancer’s invisible shield, scientists had turned one of the disease’s major advantages into a vulnerability.

“Those attributes that permit it to evade immune recognition and thrive in a host are those attributes that can be targeted in order to destroy those cancers,” he said.

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