

FIVE QUESTIONS

Cancer drug helps treat MS

Researchers and doctors hail Ocrevus as a game-changer.

By Sandy Bauers
 FOR THE INQUIRER

The quest to cure multiple sclerosis, or even to discover its cause, has remained elusive.

But in March, the U.S. Food and Drug Administration approved a new drug to treat the most severe form of the disabling neurologic condition, which causes the body's immune system to malfunction, attacking the cells of the spinal cord and brain. MS affects more than 450,000 people — more often women — in the United States.

The new drug, Ocrevus, has been hailed by researchers and physicians as a game-changer, with the potential to lead to new avenues of treatment for other diseases, as well.

One of those involved in the research and development of the drug is neurologist and scientist Amit Bar-Or, recently named chief of the multiple sclerosis division in the University of Pennsylvania's Department of Neurology, and director of the new Center for Neuroinflammation and Experimental Neurotherapeutics.

See **OCREVUS** on G3

He spoke to us recently about the new MS treatment, and why even those of us who weren't science majors will find this tale of T cells, B cells and a molecule called CD20 fascinating.

Let's start with a brief overview of

Ocrevus and how it works.

Ocrevus is an example of an anti-CD20 monoclonal antibody. Basically, it is a molecule that is able to very specifically stick to another molecule called CD20, which is expressed on the surface of B cells of the immune system. The B cells are then very quickly killed. This type of anti-CD20 therapy was approved in the U.S. in the late 1990s as a treatment for B-cell lymphoma, a type of blood cancer. It was very effective at killing and getting rid of the lymphoma B cells.

We now know, based on formal clinical trials, that Ocrevus is very effective in limiting new MS attacks. Some MS patients may say, "That's great, but I don't want to be on a cancer therapy." But there's a big difference between monoclonal antibodies against cancer and traditional chemotherapies. Traditional chemotherapies work by killing any multiplying cell. Cancer cells multiply, but so do many other cells, which is why such therapies can also give nasty side effects, such as severe nausea and hair loss. Monoclonal antibodies in cancer therapy represented a breakthrough because they targeted particular cells, thereby limiting risks and side effects. They have now been applied to conditions like MS.

What's odd is that MS has long been thought to be caused by T cells — not B cells — of the immune system. People may well ask, why should a treatment that selectively targets B cells, work so well in a T-cell disease? That's a good question. In fact, Ocrevus provides an example of how the development of a new MS treatment has taught us some very important new things about MS itself. We now know B cells play a key role in new MS attacks — and by studying Ocrevus, we have learned why.

Why are B cells so important here?

B cells are best known for making antibodies. Normally, B cells make antibodies that attack foreign invaders and help get rid of them. But B cells can sometimes make antibodies that attack our own body. We have known for many years that patients with MS have exaggerated levels of antibodies in their spinal fluid. This was the original reason for trying to treat MS patients with a B cell-directed therapy. A big surprise was the observation that the abnormal spinal fluid antibodies in patients were not changed after B cell depletion, while patients nonetheless benefited from great reductions in new attacks.



This meant that B cells were clearly involved in relapses, but because of something other than antibodies. By carefully studying patients before and after treatment, we learned that B cells of MS patients abnormally influence T cells, making them more aggressive. So MS attacks are driven by interactions between B cells and T cells, which is why eliminating B cells with Ocrevus is so effective against relapses. These discoveries — carried out in part in my lab — have contributed to an exciting evolution of our understanding of MS.

From the patients' perspective, what is this treatment like?

One of the game-changing aspects is that Ocrevus could be suitable for quite a broad range of people with relapsing MS as well as for some with primary progressive MS. It is nonetheless not for everyone, so it is important that patients be evaluated by their neurologist or MS specialist.

Another advantage is that Ocrevus is overall quite easy to tolerate. After the initial two infusions, which are administered two weeks apart, subsequent infusions are once every six months. They should be done in a certified infusion center. The infusions may cause side effects — flushing, chills and low-grade fever — due to the rapid loss of B cells. But they are generally mild to moderate, and they tend to decrease with subsequent infusions.

The cost, about \$65,000, is covered by a variety of insurance plans. If \$65,000 sounds like a lot of money — and it is — it is nonetheless in the lower range of the expensive MS treatments already approved. Some payers are still figuring out co-pays, and so on. But for the most part, coverage is unlikely to be much different from current therapies.

Does this drug have any broader implications for treating other autoimmune diseases?

Yes. Because of what we have learned in MS, there is a lot of interest in how the multiple functions of B cells may be involved in other immune-mediated conditions. The approval as a treatment for MS consolidates our understanding of these new roles, which I think will fuel further interest in this approach for other medical conditions.

What's next?

A major frontier is to better understand and treat progressive forms of MS, and to develop approaches to repair injuries that have already occurred to the nerve pathways and myelin that insulates them.

We are creating a unique across-the-age-span program jointly between Penn and the Children's Hospital of Philadelphia that seamlessly transitions care of children and adolescents into adulthood and invites all interested patients to participate in research endeavors that will further advance our understanding and treatments of people with MS.

✉ sandybauers10@gmail.com



Amit Bar-Or: "Another advantage is that Ocrevus is overall quite easy to tolerate."