CellCept® Is Superior to Azathioprine In Treatment of Lupus Nephritis

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- Ginzler EM, Appel GB, Dooley MA, Isenberg DA, Jayne D, Wofsy D, Solomons N, Lisk L, and Close DR. (2010). Aspreva Lupus Management Study (ALMS): maintenance results. American College of Rheumatology Abstracts 2085.

What is the topic?
There are a number of treatments used for lupus nephritis, but none of them are approved by the U.S. Food and Drug Administration (FDA). This is because the FDA requires a treatment to demonstrate that it is superior to placebo or standard of care before it can be approved. This involves studies where some of the patients are randomly assigned to get placebo (inactive treatment) either alone or in addition to standard of care therapy. It has been hard to figure out how to design clinical trials for nephritis that allow all the patients (including those on placebo) to receive acceptable standard of care treatments because the standard of care for this more serious type of lupus flare is very aggressive.

Previously, CellCept®, also known as mycophenolate mofetil (MMF), was compared to Cytoxan®, also known as cyclophosphamide (CYC), in a study of lupus kidney disease and they seemed to have equal effectiveness. Even though CYC is a chemotherapeutic agent, it is thought to be the same as placebo by the FDA because it is not approved for lupus and has never been shown to be effective for nephritis. It would be unethical to test either of these treatments against just placebo or a treatment that is considered weak because the placebo patients would be receiving less than the standard of care, and nephritis is too serious to set up a study like that. This seemed to be a Catch-22 and it was wondered how any treatment for nephritis could be proven effective.

After the study in which MMF was compared to CYC and found to have similar effectiveness, there was a follow-up study for those patients who had done well on either treatment. These patients were now randomly assigned to receive azathioprine (also known as Imuran) or MMF, which are both accepted standard of care treatments for what is called "maintenance therapy" – the continuation of treatments that are used after a person gets better from a bout of nephritis but it might be too early to take them off all medicine.

What did the researchers hope to learn?
The researchers hoped to compare the efficacy and safety of MMF and azathioprine as maintenance therapy for lupus patients who had responded well to a six-month, initial phase of treatment.

Who was studied?
227 people with active lupus nephritis were studied over a 36-month period after responding well to an initial six-month treatment with steroids and either MMF or CYC.

How was the study conducted?
People with active lupus nephritis received either MMF (2 grams per day) plus placebo or oral azathioprine (2 mg/kg per day) plus placebo. Patients were allowed to receive steroids (maximum dose of 10 mg/day of prednisone or equivalent, if needed). The patients in the different treatment groups had similar lupus disease characteristics.

What did the researchers find?
127 out of 227 patients completed the study. Of these, 73 were taking MMF and 54 were taking azathioprine.

The time it took to have a kidney flare was longer in patients taking MMF than in those taking azathioprine.

There were no differences in side effects in those taking either MMF or azathioprine. The most common side effects were infections and stomach or bowel disorders.

Patients had better outcomes taking MMF than azathioprine regardless of race, geographic region, or which drug they received during their initial six-month treatment for lupus nephritis (either MMF or CYC).

What were the limitations of the study?
There were a lot of people who dropped out of this study and there could be many reasons for this since it was such a long study. However, it is possible that if all the information about the patients dropping out were known, different insights might be obtained.

What do the results mean for you?
MMF is associated with longer prevention of a new kidney flare after effective treatment of the last flare compared to an effective standard of care treatment. This information might help physicians and lupus patients in making decisions about selecting treatments, but also illustrates how much more we need to know about these issues. For example, it would be good to have blood tests that could predict which patients might do just as well on azathioprine or which patients might still flare after maintenance with MMF. Even better would be tests which could predict the new flares before they happened and help to select a new treatment to prevent damage to the kidney at an earlier point.