THE
Arthritis Research
WINTER 2000
NEWSLETTER

FDA Approves Powerful Arthritis Treatment

Remicade costs covered by Medicare

In early November, Remicade™ (inflixamab) was approved by the US Food and Drug Administration (FDA) for the treatment of Rheumatoid Arthritis (RA). Like Enbrel" that was approved in late 1998, Remicade is an anti-TNF agent and, like Enbrel, it is very effective in controlling RA. Remicade is manufactured by Centocor, Inc.

TNF is a cytokine, a substance by which cells in the body communicate with each other. TNF is a strong promoter of inflammation and is one of the primary substances that produce the inflammation, pain and damage of RA. Remicade works by binding to and neutralizing TNF-alpha on the cell membrane and in the blood.

The FDA's approval of Remicade was based on findings from ATTRACT, a double-blind, placebo-controlled, randomized clinical trial involving 428 patients at 34 clinical sites. ATTRACT was one of the largest clinical studies ever conducted in patients with advanced rheumatoid arthritis.

After 30 weeks of treatment 50 percent of all patients treated with REMICADE and methotrexate, compared to 20 percent of patients receiving methotrexate alone, noted reductions in pain and swelling, and noted significant improvement in functional ability.

In a second important report, Remicade was shown to prevent X-ray damage during a one year study period. Among 285 persons with RA who received Remicade and methotrexate, no progression was noted. But among the 63 persons treated with methotrexate alone considerable X-ray joint damage was observed.

Widespread Availability

Unlike all other new medications for RA, Remicade costs will be paid by Medicare. This does not represent a change in Medicare rules, but instead reflects the fact that Remicade must be administered intravenously (by IV infusion). Because it must be given by a physician or clinic, rather than simply taken by persons with RA, Medicare rules call for full payment. And this is no small benefit. Remicade costs around $8,000 per year without adding on the costs of administration—costs that can run from several thousand to ten thousand dollars per year. Remicade, then, is the first of the new class of biologic drugs that will be available to older Americans with RA.

Remicade is given by an intravenous infusion that takes about 3 hours. After the first infusion, repeat treatments need to be given at 2 weeks and at 6 weeks. After that it should be given every 8 weeks or 6 times a year. Remicade needs to be taken with methotrexate. By virtue of its availability and its effectiveness, Remicade may move rapidly into the role as a most effective RA treatment.

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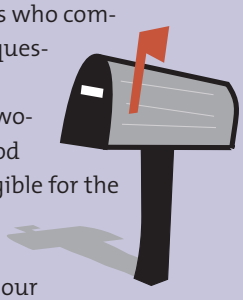
Fifty percent of all patients noted reductions in pain and swelling

WIN $1000

Return your research questionnaire within two weeks of receiving it and be eligible for one of three $1,000 awards. The research data bank can best contribute to research when the mailed questions are completed and returned as soon as possible. All persons who complete the questionnaire within a two-week period will be eligible for the award – given as a token of our gratitude in help with arthritis research. See back page for past winners.

Time is running out!



Research at the ACR

The American College of Rheumatology (ACR) met in Boston in November. A wide series of important research studies about rheumatoid arthritis, osteoarthritis and fibromyalgia were presented to rheumatologists from all over the world. Here are the highlights.

Glucosamine Reduces Progression of Knee Osteoarthritis

Glucosamine, a dietary supplement sold over the counter in the United States and as a prescription drug in Europe, reduced the signs and symptoms of osteoarthritis of the knee. "For the first time, we have shown that a compound may be able at least to slow down the progression of osteoarthritis," said lead investigator Jean-Yves Reginster, MD PhD, of the University of Liege in Belgium.

The three-year study compared disease symptoms and X-ray changes between patients taking a 1500 mg daily dose of glucosamine and those taking a placebo. Joint space narrowed (cartilage loss) in patients on placebo but showed no further narrowing in patients on glucosamine. Symptoms worsened for patients on placebo and improved for those on glucosamine.

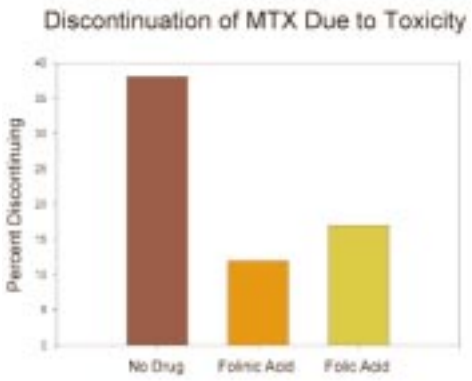
These results must be confirmed by other randomized trials, several of which are underway. A multi-center study of glucosamine sponsored by the National Institutes of Health (NIH) will begin in the US in January.

Arthrotec and Acetaminophen: a comparison in Osteoarthritis of the Hip and Knee.

A team of investigators from Vanderbilt University led by Dr. Theodore Pincus presented the results of a controlled study comparing Arthrotec', an anti-inflammatory drug (NSAID) with Acetaminophen (Tylenol'). During a 6-week trial, these researchers found acetaminophen to be less effective than the NSAID. This study is similar to one presented from the National Data Bank and describe in the last newsletter. In that study persons with RA, OA and fibromyalgia were also found to prefer NSAIDs to acetaminophen. These two studies presented evidence challenging the recommendations of the ACR that indicated that both drugs were equally effective. The two studies did note, however, that many persons found acetaminophen and NSAIDs equally effective.

Folic Acid & Methotrexate (MTX) In Rheumatoid Arthritis (RA)

Methotrexate is the most common drug treatment for RA. Some studies have suggested that taking folic acid (a vitamin) along with MTX may reduce toxicity. On the other hand, there have been worries that that using folic acid along with MTX would reduce the effectiveness of MTX. An excellent study by Van Ede and his colleagues from the Netherlands seems to have settled the question of MTX and folic acid.



As shown in the figure at right, the use of folic acid reduced toxicity from 37% to 17%. Folinic acid, a very expensive folic acid-like compound, seemed slightly more protective,

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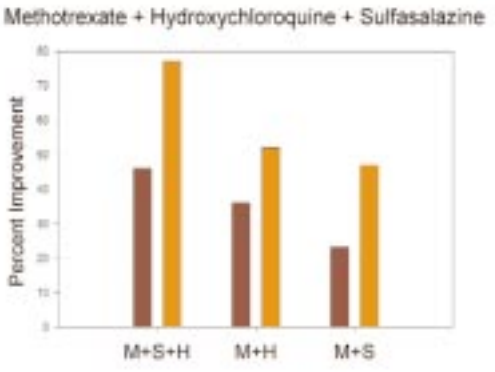
Prosorba Also Approved

Prosorba is a new and unique RA treatment that was approved by the FDA in early 1999. It is for people with RA who have severe problems that have not been controlled by usual treatments. Some people say that prosorba 'washes the blood.' More scientifically, it is a treatment that absorbs antibodies from the blood. Removing certain antibodies can lead to better control for RA.

Unfortunately Prosorba is a complex and difficult treatment that is similar to dialysis. The blood (actually plasma) is drawn out of the body, passed through a glass column that extracts the antibodies and then is returned to the body.

Although difficult and costly, it is usually covered by medical insurance, and can be of help in cases where RA is not responding to usual treatments.

although statistical analyses showed that the differences between folic acid and folinic acid were probably due to chance. Almost all of the prevented toxicity was liver toxicity. Another important finding in this study was that the use of the folic acid compounds did not reduce MTX effectiveness. Conclusion: folic acid should be used when MTX is taken for treatment of RA.



Follow-up on Triple Therapy

Several years ago Dr. James O'Dell from the University of Nebraska reported in the New England Journal of Medicine that the combination of methotrexate (M), sulfasalazine (S), and hydroxychloroquine (H) was the most effective of treatments for RA. In a new report, the Nebraska researchers compared the 3 drugs in a double-blind study using an increased dose of sulfasalazine..

77% of patients with RA had at least a 20% (orange bar) improvement on M+H+S compared with 52% on M+H, as shown in the figure above. When at least a 50% improvement (brown bar) was looked for, 46% achieved that success on M+H+S compared with 36% on M+H. M+S was not an effective combination in comparison to the others. These results suggest that the triple drug combination may be better than the two drug combinations. What is not known is how much better any of these combinations might be than methotrexate alone or even placebo alone.

Methotrexate has become the most common therapy for rheumatoid arthritis in the United States.

Methotrexate Versus Arava

Using National Data Bank data, as reported in the last issue of the newsletter and presented to the ACR November meeting, methotrexate (MTX) has become the most common therapy for RA in the United States. Early studies of ARAVA showed that it was about as effective as MTX. Two longer-term studies are now available to shed additional light on the drug comparison. Cohen and associates presented two year comparisons of ARAVA and MTX. Using the 50% improvement criteria, there was no significant difference between the drugs after two years of treatment. In a second study, Olsen and her colleagues studied RA patients who had started on either MTX or ARAVA and who had not done well on their treatment. Patients were then switched from ARAVA to MTX or from MTX to ARAVA, depending on which drug they had been on. The researchers reported that up to half of patients not responding to ARAVA or MTX responded well to the other treatment. In this instance responding 'well' meant having at least a 20% improvement.

The results of these two studies suggest that MTX and ARAVA are similar in their effectiveness. As we noted in the last newsletter, data from the National Data Bank questionnaires should soon provide real world answers to the relative effectiveness of the treatments.

Osteoarthritis: A Topical Lotion

If you have only one or a few joints that are hurting, it makes sense to try to treat them with a topical lotion or cream. That way you don't have to take oral medication with all of their potential adverse effects.

Many products contain soothing oils. Some, like capsaicin creams, contain ingredients to desensitize nerve endings. In a study presented at the ACR meeting, a group of Canadian investigators led by AM Bookman studied the effect of a nonsteroidal antiinflammatory drug (NSAID), diclofenac (Voltaren™), on pain caused by osteoarthritis of the knee. Compared to placebo and DMSO, diclofenac lotion reduced pain and improved function. NSAID lotions are used in Europe, but have not been approved in the US. Even so, this is a novel OA treatment that, perhaps, will be available here after a while.

Questions?

Contact our Research Director, Nancy Flowers by email at research@arthritis-research.org or try our web site. You can find us at www.arthritis-research.org. Postal inquiries should go to National Data Bank For Rheumatic Disease
1035 N. Emporia, Suite 288
Wichita, KS 67214

News From the National Data Bank

This has been an exciting 15 months for RA treatments. During this period Enbrel, ARAVA, Remicade, Prosorba, Celebrex and Vioxx were all released. As the millenium begins, there is new hope for persons with arthritis. In testing now are drugs that should reduce OA pain and disability, and preserve joint cartilage. Even more effective treatments are ahead in RA and fibromyalgia – perhaps only a year or two away.

The National Data Bank for Rheumatic Diseases (NDB) helps to evaluate these treatments, and their benefits and risks, in the real world. Research studies such as we have reported upon in this newsletter are fine and important, but they don't always answer the question of how well drugs work in actual practice, how well they will be tolerated, and whether we can afford them. The questionnaires that you fill out help us to do just that, and more.

NDB research is recognized as being important. At the national meeting of the American College of Rheumatology, the NDB had more abstract presentations than any other group or university in the US. During the next year data from NDB studies will be presented at the European rheumatology meeting in France, the Asian meeting in Beijing, and a South American meeting in Argentina, as well as at the 2000 meeting of the American College of Rheumatology..

So thanks, and here's a way to make $1,000

Winners!

The three winners of the summer '99 giveaway were Ouida Nelson of Louisville KY, Rosemary Bonin of Salina KS, and one person who wished to remain anonymous. Congratulations to each of these $1,000 winners. You too can be a winner. So get your questionnaire in fast. The $1,000 award is our way of saying thank you.

Three $1,000 Awards to Arthritis Research Participants

Return your research questionnaire within two weeks of receiving it and be eligible for one of three $1,000 awards. The research data bank can best contribute to research when the mailed questions are completed and returned as soon as possible. All persons who complete the questionnaire within a two weeks period of receiving it will be eligible for the award – given as a token of our gratitude in help with arthritis research.

New Study for Patients with Osteoarthritis of the Knee

The National Institutes of Health is sponsoring a multicenter clinical trial to test the effects of the dietary supplements glucosamine and chondroitin sulfate for treatment of osteoarthritis of the knee. The study will test whether glucosamine and chondroitin sulfate used separately or in combination are effective in reducing pain and improving functional ability in patients with osteoarthritis of the knee.

Here is how it will work: Patients will be randomly assigned to receive either (1) glucosamine alone, (2) chondroitin sulfate alone, (3) glucosamine and chondroitin sulfate in combination, or (4) a placebo. Each patient will be treated for 16 weeks. During this time, patients will be evaluated at monthly intervals and closely monitored for improvement of their osteoarthritis as well as for any possible adverse reactions .

The study is being coordinated by the University of Utah School of Medicine in Salt Lake City, and will be conducted at nine study centers, including our site in Wichita. Other sites around the country are: University of California at San Diego, University of California at San Francisco, Indiana Uniersity School of Medicine in Indianapolis, Case Western Reserve University in Cleveland, University of Nebraska Rheumatology Network in Omaha, University of Pennsylvania School of Medicine in Philadelphia, and Virginia Mason Medical Center in Seattle.

It is anticipated that 1,124 patients wil be recruited for the study. Recruitment is expected to begin in February 2000. Patients with knee pain and x-ray evidence of osteoarthritis are encouraged to consider participation in the study.

If you live in the Wichita area and are interested in participating in this study, please call Edie Sparr at 1-800-323-5871 ext. 117. If you live in another area where the study is being done, you may contact Diana Kucmeroski, Study Coordinator, University of Utah Schol of Medicine, 801-585-6468.