THE
Arthritis Research
SUMMER 1999 NEWSLETTER

Vioxx – the Second Cox-2 NSAID Released

What was the first NSAID?

In our last issues we introduced the new NSAID, Celebrex. Since then a new NSAID called Vioxx has been released. As background, let's repeat a little of what we wrote about drugs and about terms like NSAIDs, Cox-1 and Cox-2.

Antiinflammatory drugs can be helpful and reduce pain, swelling, cramps and fever. Examples include aspirin, Naprosyn, Aleve, Motrin, Ibuprofen, Daypro, Relafen and many more. The official name for these drugs is non-steroidal antiinflammatory drugs or NSAIDs, for short. They are called 'non-steroidal' because they don't contain steroids – that is they don't contain cortisone or prednisone. As good as they are, NSAIDs can cause problems, including stomach distress such as ulcers, stomach pain and bleeding. Many people simply can't take these drugs because of such side effects.

CELEBREX (CELECOXIB CAPSULES)

Why does this happen?

NSAIDs work by interfering with an enzyme called COX that helps produce inflammation. In recent years it was discovered that cyclooxygenase or 'COX' exists in two distinct forms – COX-1 and COX-2. Both forms reduce inflammation, but COX-1 inhibition causes stomach problems by interfering with natural protective effects in the stomach. COX-1 inhibition also can lead to kidney problems and bleeding problems. COX-2 inhibition leads to none of these problems, yet it still relieves inflammation.

Enter Celebrex.

Up until February all of the NSAIDs available in the U.S. were COX-1 drugs. However in February the first COX-2 drug was released. Developed by Searle laboratories, it is called Celebrex™ (celecoxib). Last month a 2nd COX-2 inhibitor called Vioxx, and made by Merck, Inc. was released for sale in the U.S.

Are Celebrex and Vioxx different?

Not by much! Celebrex is recommended as 200mg once a day for osteoarthritis (OA) and 100mg twice a day for rheumatoid arthritis (RA). The price for the RA dosage is higher than the price for the OA dosage. Vioxx is a once-a-day drug regardless of whether you take the 12.5 mg or the 25 mg dose. So if you need the stronger dosage, Vioxx will cost a little less.

VIOXX (rofecoxib)

Awaiting official approval

Celebrex is approved for RA and OA, but Vioxx is only approved for OA. Studies are completing for use of Vioxx in RA, and it is expected to win approval. Based on that knowledge, some doctors are using Vioxx for RA now. Since Vioxx works for pain it can be used for all musculoskeletal pain conditions, including fibromyalgia.

As to side effects, people who have allergies to sulfonamides shouldn't take Celebrex but can take Vioxx.

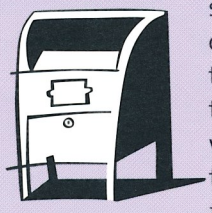
How well do they work?

We reported last time that studies performed before the drugs were released indicated that both drugs were safe and effective. The

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!



first information about how well they actually work in practice will come when we analyze your questionnaires in the next few months (so get those questionnaires in quickly, please!). But experience of rheumatologists indicate that the drugs are performing well, and there have been no unexpected side effects.

Who should take these drugs?

If you need an NSAID, the COX-2 inhibitors are the safest. So if you have had ulcers or stomach problems that made it difficult for you to use NSAIDs, or if you are older and at higher risk for stomach problems, then Celebrex or Vioxx may be for you. But, remember that Celebrex and Vioxx are no stronger than any of the older COX-1 NSAIDs and cost more than over-the-counter medications such as Aleve or ibuprofen. But if you are looking for safer medications these drugs may be what you need.

DMARDS: Arava, Enbrel and what's next?

DMARDS such as Arava and Enbrel are drugs that reduce or halt the damage caused by rheumatoid arthritis. Unlike NSAIDs that reduce arthritis symptoms almost as soon as you take them, DMARDS usually take months to work. When they start to work they reduce or stop the underlying activity of the arthritis. This reduces pain and swelling, improves function, and reduces or stops damage to joints and cartilage. When DMARDS work, they are much more powerful than NSAIDs. An analogy to use in comparing NSAIDs and DMARDs is that DMARDs are like sunscreens that prevent sunburn but NSAIDs are like sunburn lotions you apply after the sunburn. The last months of 1998 saw the release of two new DMARDS that should be of great help to people with RA. The first is called ARAVA™ (leflunomide) and the second is Enbrel™ (entanercept).

If you are looking for safer drugs, then Celebrex and Vioxx could be for you.

How well do Arava and Enbrel work?

As with the Cox-2 drugs mentioned above, we will have a pretty good idea when we analyze your current questionnaires. But so far rheumatologists' experience is that the drugs are, in fact, pretty good

Arava and the National Data Bank.

Over the last six months, almost 4,000 persons with RA who started to take Arava became participants in the National Data Bank (NDB) when they filled out short questionnaires in their rheumatologist's office at the time they received a prescription for Arava. We welcome all of you to the NDB program. With the mailing of this summer questionnaire we will be trying to find out in detail how well Arava worked by analyzing the questionnaire results from all of those who were just started on Arava. We'll let you know how it all turned out in the next newsletter.

And Enbrel?

On the basis of short-term clinical studies performed before the approval of Enbrel, it appears to be the most effective of all DMARDS.

We will also have data bank results on Enbrel soon. Remember that Enbrel alters the immunological reaction that causes inflammation by binding to the TNF receptor, thereby preventing real TNF from binding to the TNF receptor. If the receptor site is blocked then TNF cannot produce inflammation. Less inflammation, far less arthritis! TNF? TNF receptor? In case you forgot (and we expect most of you did) see the January 1999 Newsletter. If you don't have a copy, drop us a note or look on our Web Site at www.arthritis-research.org.

Rheumatologists are reporting that some of those with RA have had striking responses to Enbrel. We'll have the results soon.

Side effects?

There have been no unexpected side effects. But the biggest drawback is cost. Enbrel costs more than $13,000 per year. Most insurance companies will cover it, but if you are over 65 years of age you are out of luck. Medicare won't pay for any drugs. And health insurance policies with a 20 percent co-pay make it almost as difficult. Arava costs more than $220 per month. Since these are really good and effective drugs, you might want to consider writing to your insurance companies, state insurance commissioners, and your senators and representatives.

Remicade

This anti-TNF agent appears to be the next on the list to be approved by the FDA. It seems to be as good as Enbrel, but only needs to be taken every few months. Interestingly, because this drug is given intravenously it may be covered by health insurance, including Medicare.

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
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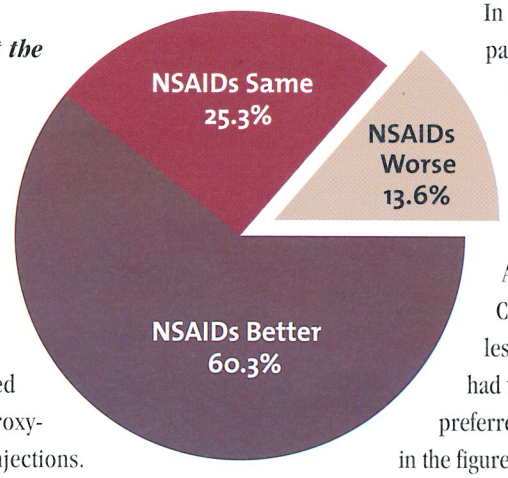
This Year's Arthritis Research Results Are In!

The results of arthritis research are usually first presented at the annual meetings of the American College of Rheumatology (ACR), which will meet this year in Boston. Researchers submit their work as 'abstracts,' short summaries of their work. If the abstracts are accepted, the researchers will then present the results at the Annual meeting. This year we submitted a large number of abstracts based on NDB work . Here are some of the results. We think you will be interested in because the results come in part from your questionnaire replies.

What was treatment for RA like at the end of 1998?

We asked 3,605 person with RA what treatments they had had over the course of their illness. When we asked the question, RA had been present for almost 9 years on average. As you can see, Almost everyone had been treated with a DMARD (94.1%). Methotrexate (MTX) was the most frequently used DMARD, followed by Plaquenil (hydroxychloroquine), sulfasalazine and gold injections. In addition, two thirds had received prednisone. But when we asked what kind of treatments were now being received, the results were different.

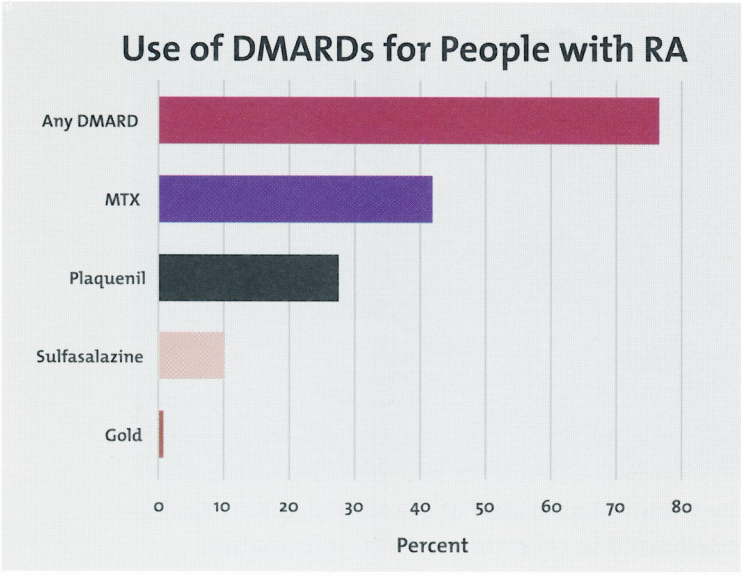
Almost no one (0.9%) was receiving gold, and 23.3% were not taking any NSAID. MTX was the most prescribed drug, followed by Plaquenil and sulfasalazine. We detected another trend. Almost 26% were taking more than 1 DMARD. This change to combination therapy reflects an increasing belief among arthritis experts that there may be more benefit in 2 drugs than in just 1. The results are not yet in for the true effectiveness of combination therapy, and the results that we determine in the NDB using your questionnaires may help to settle the question.



Better or Worse:
Acetaminophen versus NSAIDs

How does acetaminophen compare to NSAIDs?

In our research questionnaire we asked participants with RA, OA or fibromyalgia to rate the comparative effectiveness of acetaminophen and NSAIDs. Acetaminophen is sometimes known by its best selling brand, Tylenol.™ NSAIDs, of course, are drugs like Advil,™ Motrin,™ Relafen,™ Celebrex,™ and many others. Regardless of diagnosis, the 1,799 persons who had used acetaminophen indicated that they preferred NSAIDs by a large margin, as shown in the figure above. This was true even when safety and effectiveness were both considered. Considering the heavy advertising of these drugs, it is important to get the perspective of those who take the medications. Score one for the NSAIDs. Does that mean you should not use acetaminophen? Not at all. For almost 40%, acetaminophen was as good or better than NSAIDs. So take the medication that works best for you. The importance of these study results is that many medical organizations had been suggesting that acetaminophen was as good as NSAIDs. Based on your response, that doesn't seem to be the case.



How common are side effects?

We reviewed questionnaires and clinic experience to try to answer this question. Among 638 RA patients and 163 with OA, approximately 15% of clinic visits were associated with a side effect to treatment.

GI or 'stomach' side effects were most common, followed by rashes, mouth and throat problems, and dizziness or fatigue. About half of those with side effects stopped taking the drug, and about 6% went to the hospital, usually for tests involving stomach problems. Overall, most side effects were not medically important since they disappeared on stopping the drug that caused the side effect.

What is a data bank?

It is a computerized record of tests, treatments, results and individual facts about each person with arthritis. From these data it is possible to see the forces that produce the outcomes of arthritis: outcomes that include pain, joint damage and the ability to work and function. With such a data bank we can identify those factors that lead to better outcomes.

For a data bank to work the data must be absolutely confidential. We make sure that only the research staff can see your identifying data. They look at the questionnaire to see if it is complete and to make sure that your name and address are correct for mailing. Once your information is in our research data bank your name is removed for research purposes. That is, any researcher using the data bank for medical research cannot identify you. Your name and medical information will not be available to any one else. We do not give away names or sell them, or make them available to anyone else. We have been collecting arthritis data for more than 25 years, and during that time no outside person has ever had access to anyone's name. No one ever will.

WINNERS!

The three winners of the winter spring giveaway were Karen Ashbaugh of Ellis, Kansas, Lucy DelGrosso of Latham, New York, and Grace Trapp of Michigan. Congratulations to all 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.

Using and sharing the data.

The purpose of the data bank is to do research about arthritis that will improve the lives of persons with arthritis. To do this we share the data with other researchers outside of the NDB staff. As we indicated above, all identifiers are removed when we do this. Just as an example, we shared data with researchers in England to explore the possible relationship between arthritis and cancer, and we shared NDB data among researchers in the US, United Kingdom, Switzerland and the Netherlands in an effort to develop better methods to measure function. The three major experts in x-rays in RA in the US and Europe have all cooperated in x-ray studies with us using data bank data, and major experts in OA x-rays have also used our data. The best way to improve research is to share data. That is one of the major goals of the National Data Bank.

Questions about the data bank? Call us, send email or see our web site.

You can always call us for questions about the NBD research (1-800-323-5871). Our email address is research@arthritis-research.org. A really good way to find out information about the NDB is to look at our web site. You can find us at www.arthritis-research.org . The web site has information that may be of interest to you. There are the frequently asked questions (FAQs) with the answers, and list of the research publications from our data bank research. Some of the forms that we use in research questionnaires will be posted there for doctors to use and for you to see. There will even be actual research papers and results of presentations of data bank research that were made at national and international meetings. Try it out, and let us know if you want anything else placed on the web site.

Current activities: Important results from current data bank research

At the annual meeting of the American College of rheumatology, Dr. Wolfe presented results from the analysis of 25 years of data-bank research in two separate plenary presentations. In the first, data bank research showed that methotrexate (MTX) was associated with increased life expectancy. The second study showed that MTX did not cause lymphoma (a form of cancer). These two studies were important because the showed that MTX was safe and that the worries regarding possible long-term side effects were unfounded. In fact, people receiving MTX did better than those who did not receive it.

The Wichita-based staff of the National Data Bank is dedicated to collecting arthritis information.