

Concluding Remarks by Pfizer: Joseph Feczko MD

JOINT MEETING OF THE ARTHRITIS ADVISORY COMMITTEE AND THE DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE

February 16-18, 2005, Hilton Gaithersburg, 620 Perry Parkway, Gaithersburg, Maryland.

Highlights.....	1
Presentation Text.....	2

Highlights

- **PATIENTS WITH CHRONIC PAIN NEED TREATMENT:** In the treatment of arthritis, “placebo is really not an alternative”. Arthritis patients need therapeutic options. “Not everything works for everyone.”
- **CARDIOVASCULAR SAFETY OF NON-SELECTIVE NSAIDS IS UNKNOWN:** Non-selective NSAIDs have known GI risks, but their long-term cardiovascular safety (compared with placebo or no therapy) has not been established.
- **CARDIOVASCULAR SAFETY OF CELECOXIB IS COMPARABLE TO NON-SELECTIVE NSAIDS:** Pfizer believes that “the cardiovascular safety of celecoxib is at least on a par with therapeutic alternatives such as the non-selective NSAIDs”.
- **A LARGE CARDIOVASCULAR SAFETY STUDY OF CELECOXIB AND NON-SELECTIVE NSAIDS IS PLANNED:** Pfizer is committed to performing a study to establish the comparability of the cardiovascular safety of celecoxib with non-selective NSAIDs. A protocol has been discussed with outside cardiologists and is currently filed with FDA.
- **EVALUATION OF CELECOXIB IN CANCER WILL CONTINUE:** Pfizer is also committed to continuing evaluation of celecoxib in cancer.
- **VALDECOXIB IS SAFE OUTSIDE A VASCULAR SURGERY SETTING:** The valdecoxib database is smaller than with celecoxib but no increase in cardiovascular risk has been seen outside the CABG surgery setting.
- **PARECOXIB IS EFFECTIVE AND SAFE OUTSIDE A VASCULAR SURGERY SETTING:** Parecoxib is a “highly effective” parenteral drug which appears to be safe in a setting of non-vascular surgery.

Presentation Text

Thank you, I will be brief. I would like to thank the panel and the FDA for the opportunity given to Pfizer today to show the data that demonstrates the cardiovascular safety profile of our COX-2 inhibitors, both Celebrex, Bextra and parecoxib.

Patients with chronic inflammatory arthritis pain have few therapeutic alternatives. While there has been a lot of debate about the placebo-controlled trials in the treatment of arthritis, placebo is really not an alternative. So, we did focus today's presentation predominantly on relative risk versus traditional non-selective non-steroidal anti-inflammatory drugs.

We know about the GI risks of older non-selective NSAIDs, but how much do we really know about their long-term cardiovascular safety? I think it is a question that needs to be answered.

Part of the problem we had, as noted in the CLASS trial, was the high dropout rate associated with diclofenac over the dosing period. Given these unanswered questions, all the data suggests that Celebrex and Bextra probably have an important role to play in treatment of patients with rheumatoid arthritis and osteoarthritis.

As you heard, there is an extensive body of clinical trial and observational data with Celebrex. We believe that this data shows that the cardiovascular safety of Celebrex is at least on a par with therapeutic alternatives such as the non-selective NSAIDs. Pfizer is committed to doing the right studies with the appropriate study population and the

appropriate study hypothesis to confirm what we believe is the preponderance of data we have seen today that Celebrex cardiovascular safety is comparable to the non-selective NSAIDs.

The Celebrex protocol is currently filed with the agency. We have had one review with a number of outside cardiology consultants. We are awaiting, however, the outcome of this advisory committee to determine whether or not the protocol, in conjunction with the FDA, is the appropriate model to be used for long-term evaluation of Celebrex.

We are committed to also continuing the evaluation of Celebrex in the prevention and treatment of cancer, as outlined by Dr. Hawk and Dr. Levin.

We also agree with Dr. Hawk, and as Dr. Furberg mentioned earlier, that I think there is a large body of evidence right now at the NIH that has already had a number of patients treated for well over two to three years, mainly in the cancer setting, mainly in placebo-controlled trials. I think it is imperative that we look at that data as soon as possible.

While the data for Bextra is definitely smaller, it is growing and in the treatment of rheumatoid and osteoarthritis we believe has not shown any increased risk in cardiovascular risk. The extrapolation from the CABG studies has been taken as evidence that there is a problem with Bextra overall. We actually don't see that right now, however, I will be the first to say that the database is much, much smaller. We are also committed to looking at Bextra in a long-term trial in our arthritis patients as

appropriate to evaluate the relative risk associated with Bextra. I think this is important because I do think rheumatoid and osteoarthritis patients do need treatment options and I will be getting to that in a second.

Parecoxib, as was just mentioned, is an injectable drug, approved and marketed in some 40 countries around the world. It has found a place in those countries in the perioperative analgesia setting. It is found to be highly effective in relieving postoperative pain and in morphine sparing and, therefore, sparing the side effects associated with morphine in the postoperative setting, such as ileus and respiratory depression. It has shown no evidence of the increase in severe AEs in the general surgery setting or the outpatient surgery setting. These seem to be confined right now to the post-CABG setting and, as Ken mentioned, this is already in the labels in all those countries in which it is currently being used and is still on the market.

In conclusion, I continue to be confident that Celebrex and Bextra have important treatment options for arthritis patients. I actually believe that there is no effective treatment for arthritis patients that is safer than Celebrex. I agree though that we do need to do the long-term evaluations of both Celebrex and Bextra to really see their place in the therapeutic armamentarium.

For arthritis patients, and here I include myself because I also am on chronic therapy for osteoarthritis--arthritis patients need safe and effective treatment options. Not everything works for everyone. Patients do try different therapeutic options and do not tolerate some and it is not really clear why. We

discussed this fact earlier on about dyspepsia, people stopping therapies, people trying various proton pump inhibitors to suppress the dyspepsia or related GI effects and these don't often work in people. Arthritis patients do need safe and effective treatments and they need to move, to work and to make the most out of each day.

So, with this, I want to thank the committee and the FDA and we will throw this open again to questions for Ken and anybody else who can answer them.

Thank you.