

Committee Questions to Dr. Witter on Celecoxib

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

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Highlights

- **APC TRIAL NOT DISCUSSED:** Dr. Wood's expressed surprise that the FDA presentation had also not discussed the APC trial.
- **STUDY IQ5-97-02-001 ADJUDICATION:** Dr. Fleming expressed concern about the adjudication process in the IQ5-97-02-001 study in which "it is certainly noteworthy that there is a pretty consistent excess across all of these key categories for Celebrex". "It is kind of hard to adjudicate something in a blinded way when all the events are in the one arm". Dr. White (Pfizer consultant) said "The adjudication committee was not aware of the results when they looked at the data at all."
- **STUDY IQ5-97-02-001 P-VALUE:** Dr. Nissen asked Dr. Fleming if he had calculated a p value for an endpoint of "APTC-like or just the serious AEs" in the IQ5-97-02-001 trial. Dr. Fleming said that it would be "probably borderline". *<Note by TMT: a Fisher's Exact Test on celecoxib (11/285) versus placebo (3/140) on "Any CV Event" gives a 2-sided p value of 0.5638 so that the basis for the Pfizer study report statement of a "statistically significant difference favoring placebo in adverse events" remains unclear.>*

Discussion Text

DR. WOOD: Thanks a lot. You also have not covered the APC trial. Right? That is sort of surprising. Does the committee want to go on to the next two presentations and wait for questions to Dr. Witter at that point? Let's do that. Let's go on to the next two presentations.

DR. FLEMING: Could I have just one?

DR. WOOD: Sorry.

DR. FLEMING: Just on slide 35 as you were presenting those 001 results, it is certainly noteworthy that there is a pretty consistent excess across all of these key categories for Celebrex. We talked, for example, about heart failure

adjudication. It is kind of hard to adjudicate something in a blinded way when all the events are in the one arm. I don't know if the adjudication committee was aware of how the results broke out before they did their adjudication. In any event, we were told those broke out at 1/1 after adjudication. They were 5/0 before. So, that seems difficult to justify as well. So, I look at this as one of a small number of placebo-controlled trials with a fairly long period or treatment exposures. So, this is of some relevance.

DR. NISSEN: Tom, did you attempt to do a p value there from those numbers?

DR. FLEMING: For which aspect of this?

DR. NISSEN: Well, say, APTC-like or just the serious AEs? Is that going to be significant?

DR. FLEMING: Probably borderline.

DR. WOOD: You know, the elephant in the room is the next trial so let's move on and see if we can get some of these questions dealt with afterwards. Let's go on to Dr. Hawk's presentation.

DR. WHITE: Do you mind if I make one comment, jut for clearing the air? The adjudication committee was not aware of the results when they looked at the data at all.

DR. WOOD: Right. Let's come back to that point later because there are lots of problems with that adjudication. Let's go on to the next two talks.