John H Holcombe

10/10/2000 10:09 AM

To: Robert W Baker/AM/LLY@Lilly, Charles M Beasley Jr/AM/LLY@Lilly
cc: Christopher C Bomba/AM/LLY@LILLY, Alan Breier/AM/LLY@Lilly, Thomas M Brodie/AM/LLY@Lilly, Patrizia Cavazzoni/AM/LLY@Lilly, James B Gregory/AM/LLY@Lilly, Hunter Heath/AM/LLY@Lilly, Jack E Jordan/AM/LLY@Lilly, Suni Keeling/AM/LLY@LILLY, Bruce Kinon/AM/LLY@Lilly, Michael B Murray/AM/LLY@LILLY, John R Richards/AM/LLY@Lilly, Eugene R Thiem/AM/LLY@LILLY, Mauricio F Tohen/AM/LLY@Lilly, Paula T Trzepacz/AM/LLY@Lilly
Subject: Re: meeting with endocrinologic consultants

Charles and Robert,
Let me add my 2 cents worth. I know our endocrine advisory group well, and I might be able to help interpret their reactions to the data presented.

First, I have attached two simple tables that the ADA uses for diagnostic cutoff points for glucose values. I show this so that we are all on the same page. The tables represent the 'world' of diagnoses in the eyes of our consultants, so we had a mismatch between the analysis (>160 for IGT) and the diagnostic criteria, while >200 is diagnostic of diabetes IF symptoms are also present. At any rate, the ADA says that a blood glucose 140 or greater should be further evaluated. As you know, the consultants wanted to see ALL glucose values at baseline and over time. Showing a large number of values of >140 at baseline will underscore the likelihood that diabetes may already be present in many patients with schizophrenia, which is another point we want to further explore and emphasize. From the data shown, the group did not agree with the premise that DM has a higher than normal prevalence in schizophrenia.

Secondly, only one endo referred to Rezulin, while others said that the present analysis had nothing in common with that drug. The point was that Lilly has to be forthcoming with the data to gain and maintain our just credibility. Showing our advisory group a slightly modified analysis with ALL glucose values would be a vital step forward here.

Thirdly, our analyses with the reference ranges from Covance raised some concern, such as a glucose of > 200 being "within the reference range for random glucose of normal individuals". I don't recall the specific value, but the 99th centile cutoff point you mentioned in the reference range was a glucose value that is 'diabetic' by any standard. I am looking into the glucose reference ranges at Covance as a result of the meeting, as clearly people with diabetes are included in the normal reference ranges.

Lastly, as others have pointed out, my sense was that the group was more concerned about weight gain than the hyperglycemia. In response to a consultant's question, the mention of weight gain in healthy volunteers at the end of the presentation, without showing the data, came as quite a surprise. It nearly appeared that this tidbit had to be drawn out of Lilly, which seemed to heighten the other questions.

We are at a critical point here. Our advisory group is Who's Who in diabetes. If we can bring a few of them to Lilly as consultants to the Zyprexa team, show them that we listened to their suggestions by presenting another analysis that THEY suggested, we should be able to solidify their support and understanding.

I am willing to work with your group in whatever capacity I can.

John

glucose values.doc

ZY 2224 245