Unknown

From: Schwartz, Jack A
Sent: Monday, November 17, 2003 12:04 PM
To: Shaw, Joan; Repp, Edward; Mullen, Jamie A; Marklund, Maja; Brecher, Martin; Jones, Martin AM (Seroquel); Lloyd (Washington), Lisa M; Wilson, Ellis; Limp, Gerald L
Cc: Tugend, Georgia L
Subject: November 13,2003 Teleconference Henry Nasrallah

Georgia Tugend and I held a teleconference with Dr. Henry Nasrallah on Thursday, November 13, 2003 to seek his input on the trial 125 design/endpoints.

We went through the primary and secondary endpoints with him. He felt the study was strong and adequately powered. He indicated that this would provide sound data opposite risperidone and especially olanzapine. His main comments were:

1. He thought the primary endpoint of OGTT was good. He suggested a number of other secondary endpoints: Leptin levels, insulin resistance, TNF-alpha, free fatty acids, resiten (?) and adiponectin. He indicated these secondary enpoints may provide good divergence trends between SQL and OLZ..

2. Ensure the three study arms are balanced in terms of demography. Lilly will criticize the study if it is not. There won't be many black patients as the study will conducted in Europe. Considering the high incidence of diabetes in the black population, the study may not be representative of the paptient population found in the US. I didn't mentioned South Africa would participate in the study.

3. He suggested considering exclusion of patients who have a primary family member with diabetes

4. Consider using fasting plasma glucose >_ 110mg/dl, inview of the new guidelines which will soon be published.

5. What happens to patients when their glucose rises above 126mg/dl? Do they continue in the study? If not, enroll them in a follow on and treat then according to a clincal guideline basis with either resperidine or queteipine. He emphatically stated that SQL revereses diabetes in patients that develop it while on OLZ therapy.

We did inform him of the situation regarding the diabetes class warning and that feedback from the FDA indicated they were firm that all atypical manufacturers would be required to have this class labeling. We informed him that Risperdal consta has received the diabetes class warning, although it is slight variant from the FDA proposed text which Lilly has already incorporated. We informed him that we included the diabetes class warning in our label so as not to delay the bipolar mania approval and it is almost verbatim that of Janssen's.

Georgia had recently visited the University of Cincinnati and discovered Keck, Strakowski, McElroy, and others are starting a metabolism ISS (sponsored with a $650K grant from Lilly) examing SEROQUEL, risperidone olanzapine and abilify. Trial size is approximately 600 patients.

Thanks,

Georgia and Jack