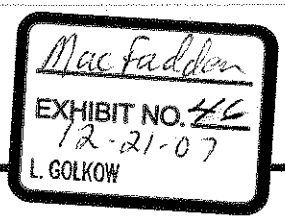

Unknown

From: Brecher, Martin
Sent: Saturday, December 18, 2004 10:03 AM
To: Macfadden, Wayne; Melville, Margaret G; Gaddy, James; Shaw, Joan; Schwartz, Jack A; McCormack, Eileen; Jones, Martin AM (Seroquel); Dunscombe, Nick M
Cc: Nordstrom, Eva (Seroquel)
Subject: RE: Trial 31 Position

Folks,
I think a short, fair balanced summary can be written using the 5 bolded statements. However, dose information MUST be reviewed and probably included before sending out.
Martin

-----Original Message-----
From: Macfadden, Wayne
Sent: Friday, December 17, 2004 12:14 PM
To: Melville, Margaret G; Gaddy, James; Shaw, Joan; Brecher, Martin; Schwartz, Jack A; McCormack, Eileen; Jones, Martin AM (Seroquel); Dunscombe, Nick M
Subject: RE: Trial 31 Position

All,

The CSR has been populated by a vendor with the methods of the trial, but not the results. After a review of the data tables in GEL, here is a quick summary of the trial and top line results. If preferred, I can shrink to a few sentences for Dr. Citrome & other investigators.:

#31 was entitled, "A Multicenter, Double-Blind, Randomized, Comparison of Seroquel and Chlorpromazine in the Treatment of Subjects with Treatment-Resistant Schizophrenia".

28 US sites, 2 Canadian sites. Patients were treated with Haldol, up to 40mg/ day for 4 weeks; non responders were randomized to receive Seroquel (N=125) or chlorpromazine (N= 128) for 10 additional weeks. Doses were flexible, up to 750 mg with SQL, up to 1500mg with CPZ.

The primary objectives were efficacy comparisons of the two treatments:

1. Response to treatment, defined as 30% or greater decrease from baseline in the Brief Psychiatric Rating Scale (BPRS) total score AND a Clinical Global Impression (CGI) Severity of Illness score of 3 (mildly ill) or less or a BPRS total score of 17 or less after treatment.

With this criteria, **the response to treatment was low in both groups; 8% of patients met this criteria in the SQL group, 7% in the CPZ group (NS)**

2. Change from baseline in the BPRS total score: **The LOCF, ITT analysis revealed an improvement of -3.11 in the SQL grouop, -7.22 in the CPZ group [more negative scores indicate higher improvement from baseline] (p=0.011)**

Further analyses showed **the BPRS positive symptom cluster was also significant for CPZ (p= 0.04) but the negative symptom score was significant in favor of SQL (p= 0.029)**

3. Change from baseline in the CGI Severity of Illness score: The LOCF, ITT analysis revealed scores of 4.09 in the SQL group, 3.58 in the CPZ group [lower scores indicate lower disease severity] (p=0.004)

Other scales for which significance testing was done:

SANS Scale for the Assessment of Negative Symptoms: NS

Simpson: NS

NOSIE (Nurses' Observation Scale for Inpatient Evaluation) p= 0.003, favoring CPZ

AIMS: p=0.059, favoring SQL

In summary, SQL and CPZ both achieved similar low levels of response in this treatment refractory population. Total, and positive subscale BPRS change scores demonstrated a statistically signifinct advantage for CPZ, negative BPRS subscale for SQL. Higher doses of SQL may have been necessary to achieve comparable results with the high CPZ dosages.

Please let me know if you'd like more detail on the above, or any other data from the tables

regards

Wayne

-----Original Message-----

From: Melville, Margaret G
Sent: Tuesday, December 14, 2004 7:03 PM
To: Macfadden, Wayne; Gaddy, James; Shaw, Joan; Brecher, Martin; Schwartz, Jack A; McCormack, Eileen; Jones, Martin AM (Seroquel); Dunscombe, Nick M
Subject: FW: Trial 31 Position

Dear All,

I have spoken to Jack about Dr. Citrome's request to have information regarding Trial 31. It is likely these data will be published on the AZ Clinical Trials Register, but as I understand it SET will take the decision this week. Jack does not believe it's appropriate to wait until these data are disseminated via that route (I believe the company intends the website to be active mid 2005).

Jim gave me a quick update by voicemail (thank you Jim) that there were some outstanding stats and that the CSR is pending. He told me that you, Wayne, were the responsible physician.

At this point, I think that we should do the following:

- Wayne, put together three to four sentences describing the high-level results
- MB/Wayne get this agreed by commercial (Nick Dunscombe or Eileen McCormack)
- Provide the summary to Dr. Citrome (Jack Schwartz) before holidays commence?

If you have disagreements to this proposal please come prepared to voice them in our Thursday am teleconference from 8-9 -- Martin Jones can give you the timings.

Best Regards,

Margaret (Meg) Melville
Seroquel Acting GPD
☎ (302) 886-2118 or 1(800) 456-3669 X 62118
mobile REDACTED

fax (302) 886-1400
margaret.melville@astrazeneca

-----Original Message-----
From: Schwartz, Jack A
Sent: Thursday, December 02, 2004 4:09 PM
To: Jones, Martin AM (Seroquel)
Cc: Brecher, Martin; Mueller, Karin; Melville, Margaret G; Beamish, Don G
Subject: Trial 31 Position

Martin,

Per my e-mail of three weeks ago, can we please add 'trial 31 position' to the agenda for the next GPT meeting. Dr. Citrome was an investigator on trial 31 and has been repeatedly asking for information on this trial. Dr. Citrome is also writing an article on atypicals and diabetes and I believe it would be in our best interest to rapidly respond to the request. I don't want to irritate him nor give him the impression that we are hiding data.
<< Message: FW: Quetiapine study >>

Thanks,
Jack