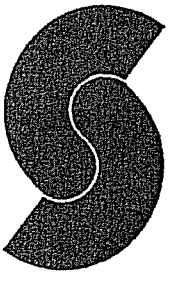
EXHIBIT 3

AstraZeneca Pharmaceuticals

Seroquel™
(Quetiapine)



Commercial Support Team - Technical Document (TD005)

CGI - Severity of Illness Meta-Analysis

Request From: Debbie Holdsworth

Date Requested: Jan 2000

Statistician/Statistical Programmer Responsible: Rob Hemmings

1 Source of Data

This document summarises initial findings into a meta-analysis of CGI - Severity of Illnes (SoI) scores taken from trials 5077IL/0013, 14, 50 and 52. As with all meta-analyses, care is required in choosing which combinations of trials can sensibly be interpreted. The data below comprises all our comparative data with Haloperidol (with the exception of trial 5077IL/0015 which assessed a significantly different patient population) and as such combines slightly different patient populations, inclusion / exclusion criterion, timings of endpoints, and doses of drug. This seems acceptable however, in order look for a general claim of superior efficacy for Seroquel over Haloperidol with regards CGI - SoI.

Any analysis of this data would be post-hoc.

2 Design of Trials/ Analysis Methods

2.1 Study Design

Table 1 gives a summary of the trials used and the pertinent design features from each trial.

Table 1

TRIAL	Treatments / Dose (# pats.)	Patient population	Inc/Exc criteria	Timing of endpoint
52 (PRIZE)	SER 600mg/day BD HAL 20mg/day BD (330 in total, 1:1 rand)	Schiz. pats. with history of partial response to trad anti-psychotic therapies	CGI, SoI >= 3	8 weeks after baseline
50 (ESTO)	SER up to 600mg/day BD HAL up to 20mg/day BD (190 in each tmt group)	Patients presenting with acute exacerbation of schiz. or schiz. disorder in last 3 years	CGI, SoI >= 4	12 weeks after baseline (also 24 and 52 weeks after baseline)
14	SER up to 800 mg/day BD HAL up to 16 mg/day BD (220 per group)	Acute exacerbation of subchronic or chronic schiz.	CGI, SoI >= 4	6 weeks after baseline
13	SER 75, 150, 300, 600, 750 mg/day TD HAL 12 mg/day TD PLACEBO (50 pats. per arm)	Hosp. patients with acute exacerbation of chronic or sub-chronic schiz.	CGI, SoI >= 4	6 weeks after baseline

Points to note are:

- Differing doses of SER and HAL across the trials;
- Slightly different patient populations (especially 52);
- Differing times of endpoint assessment.
- Data from the 75mg/day group has been excluded from trial 0013 as it is not in the therapeutic dose range for Seroquel.

2.2 Analysis Methods

Only descriptive summaries have been performed on this combined data. The only assumption made is that results can be sensibly interpreted when data from these trials are combined.

2.3 Details of SAS programs

Analysis programs from trials 13 and 14 are stored in the CDE under the CST directory (s:\d5077\filesm\CST) in two programs named TD5_G1 and TD5_G2. Analysis programs from trials 50 and 52 are in the CDE under the trial directory and are named as above.

3 Results

Before the data from these trials was considered for analysis, they were explored using standard summary statistics. The endpoints requested to be explored were: Change from baseline in Severity of Illness; and Proportion of patients with Severity of Illness ≤ 3 at endpoint.

Table T1 (Appendix A) shows the results of these summaries. Using either endpoint definition, it is clear that a claim of superiority for Seroquel over Haloperidol could not be generated using these data as the Haloperidol arm has a greater proportion of patients with lower CGI-SoI at endpoint and with greater reductions from baseline. It is noted, however, that a claim of 'equivalence' may be possible, given a prospective definition of clinical equivalence limits.

It was feared that messages from these trials may have been diluted by combining low and high doses of Seroquel. Therefore data from trials 13, 14, 15 and 50 were further explored, by taking only the following data:

Table 2 - Definition of 'High' doses of Seroquel for each of the trials

TRIAL	mg/day	
13	>= 600	i.e. ignoring the 75, 150 and 300 mg/day categories
14	>= 450	
50	>=450	
52	600	i.e. all available data

Results from these additional explorations are summarised in table T2 Appendix A (in addition, dose response results from trial 13 is summarised in Appendix B below). They do not suggest any different conclusions to those described above, i.e. that a claim of superiority is highly unlikely using these definitions, whilst a claim of equivalence is not ruled out.

A final hypothesis examined was that the effect of Seroquel relative to Haloperidol may be larger in patients with severe disease at baseline. Tables T3 and T4 in Appendix A are repeats of table T1 but for patients with baseline severity of 3-5 and 6,7 respectively.

4 Conclusions

The intended claim of 'superiority versus Haloperidol' is highly unlikely using these data, however a claim of equivalence is not ruled out.

5 References

None

Appendix A: Statistical Appendix

Index of Tables Created

TABLE T1 Change from baseline and level of severity at endpoint in CGI-SoI scores

Change from baseline in severity	TRIAL 13*		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
-5	1	0	2	0	0	0	0	0	3	0	0.4	0
-4	0	1	4	12	4	5	2	1	10	19	1.5	3.5
-3	9	2	20	25	17	18	5	5	51	50	7.5	9.3
-2	22	8	44	53	26	33	21	14	113	108	16.6	20.0
-1	63	13	68	58	60	54	35	35	226	160	33.3	29.6
0	82	22	49	55	30	39	34	54	195	170	28.7	31.5
1	22	4	30	9	9	5	11	7	72	25	10.6	4.6
2	5	0	2	7	0	0	1	1	8	8	1.1	1.5
3	0	0	1	0	0	0	0	0	1	0	0.1	0
4	0	0	0	0	0	0	0	0	0	0	0	0
									679	540	100.00	100.00

Level of severity at endpoint	TRIAL 13*		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
1	2	0	5	8	6	4	3	3	16	15	2.4	2.8
2	14	5	29	33	10	20	15	8	68	66	10.0	12.2
3	39	7	53	52	38	42	35	31	165	132	24.3	24.4
4	58	16	46	58	55	44	36	46	185	164	27.2	30.4
5	44	14	42	36	26	36	10	21	122	107	18.0	19.8
6	47	5	35	28	9	7	9	7	100	47	14.7	8.7
7	10	3	10	4	2	1	1	1	23	9	3.4	1.7
									679	540	100.00	100.00

* Doses of SER have been combined - 75mg group has been excluded

TABLE T2 Change from baseline and level of severity at endpoint in CGI-SoI scores (high doses of Seroquel only)

Change from baseline in severity	TRIAL 13		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
-5	0	0	0	0	0	0	0	0	0	0	0	0
-4	0	1	0	12	2	5	2	1	4	19	1.3	3.5
-3	2	2	2	25	4	18	5	5	13	50	4.1	9.3
-2	13	8	14	53	5	33	21	14	53	108	16.9	20.0
-1	34	13	20	58	12	54	35	35	101	160	32.2	29.6
0	40	22	17	55	11	39	34	54	102	170	32.5	31.5
1	14	4	10	9	3	5	11	7	38	25	12.1	4.6
2	2	0	0	7	0	0	1	1	3	8	0.1	1.5
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
									314	540	100	100

Level of severity at endpoint	TRIAL 13		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
				n			n	n	n	n	n	n
1	0	0	0	8	2	4	3	3	5	15	1.6	2.8
2	8	5	2	33	2	20	15	8	27	66	8.6	12.2
3	20	7	19	52	8	42	35	31	82	132	26.1	24.4
4	24	16	13	58	14	44	36	46	87	164	27.7	30.4
5	25	14	13	36	7	36	10	21	55	107	17.5	19.8
6	22	5	14	28	3	7	9	7	48	47	15.3	8.7
7	6	3	2	4	1	1	1	1	10	9	3.2	1.7
									314	540	100	100

TABLE T3 Change from baseline and level of severity at endpoint in CGI-SoI scores (patients with baseline score of 3, 4 or 5)

Change from baseline in severity	TRIAL 13*		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
-5	0	0	0	0	0	0	0	0	0	0	0	0
-4	0	0	2	5	3	4	2	1	7	10	1.3	2.4
-3	7	1	16	14	7	9	4	5	34	29	6.5	6.9
-2	19	6	38	39	15	26	18	13	90	84	17.3	20.0
-1	48	9	56	46	49	44	32	31	185	130	35.6	30.9
0	51	17	30	37	24	33	30	50	135	137	26.0	32.5
1	18	2	24	9	7	5	11	7	60	23	11.5	5.5
2	5	0	2	7	0	0	1	1	8	8	1.5	1.9
3	0	0	1	0	0	0	0	0	1	0	0.2	0
4	0	0	0	0	0	0	0	0	0	0	0	0
									520	421	100.00	100.00

Level of severity at endpoint	TRIAL 13*		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
1	1	0	3	8	6	4	3	3	13	15	2.5	3.6
2	14	4	27	26	9	19	15	8	65	57	12.5	13.5
3	37	6	49	41	28	33	34	31	148	113	28.5	26.8
4	45	14	41	44	44	37	33	46	163	141	31.3	33.5
5	32	10	29	25	15	26	7	16	83	77	16.0	18.3
6	18	1	19	10	3	2	6	4	46	15	8.8	3.6
7	1	0	1	3	0	0	0	0	2	3	0.4	0.7
									520	421	100.00	100.00

* Doses of SER have been combined - 75mg group has been excluded

TABLE T4 Change from baseline and level of severity at endpoint in CGI-SoI scores (patients with baseline score of 6,7)

Change from baseline in severity	TRIAL 13*		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
-5	1	0	2	0	0	0	0	0	3	0	1.9	0
-4	0	1	2	7	1	1	0	0	3	9	1.9	7.6
-3	2	1	4	11	10	9	1	0	17	21	10.7	17.6
-2	3	2	6	14	11	7	3	1	23	24	14.5	20.2
-1	15	4	12	12	11	10	3	4	41	30	25.8	25.2
0	31	5	19	18	6	6	4	4	60	33	37.7	27.7
1	4	2	6	0	2	0	0	0	12	2	7.5	1.7
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
									159	119	100.00	100.00

Level of severity at endpoint	TRIAL 13*		TRIAL 14		TRIAL 50		TRIAL 52		TOTAL n		TOTAL %	
	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL	SER	HAL
	n	n	n	n	n	n	n	n	n	n	n	n
1	1	0	2	0	0	0	0	0	3	0	1.9	0
2	0	1	2	7	1	1	0	0	3	9	1.9	7.6
3	2	1	4	11	10	9	1	0	17	21	10.7	17.6
4	3	2	5	14	11	7	3	0	22	23	13.8	19.3
5	12	4	13	11	11	10	3	5	39	30	24.5	25.2
6	29	4	16	18	6	5	3	3	54	30	34.0	25.2
7	9	3	9	1	2	1	1	1	21	6	13.2	5.0
									159	119	100.00	100.00

* Doses of SER have been combined - 75mg group has been excluded

Appendix B: Supporting Presentations

TABLE T5 - CGI-Sol Trial 0013

Level of severity at endpoint	DOSE (mg/day) SER 150	SER 300	SER 600	SER 750	HAL 12	PLA
	n	n	n	n	n	n
1	0	2	0	0	0	0
2	1	5	7	1	5	1
3	14	5	8	12	7	3
4	9	15	10	14	16	11
5	9	10	13	12	14	16
6	13	12	8	14	5	12
7	2	2	5	1	3	8

Change from baseline in severity	DOSE (mg/day) SER 150	SER 300	SER 600	SER 750	HAL 12	PLA
	n	n	n	n	n	n
-5	0	1	0	0	0	0
-4	0	0	0	0	1	0
-3	3	4	2	0	2	0
-2	4	5	7	6	8	2
-1	13	16	14	20	13	7
0	23	19	19	21	22	24
1	3	5	7	7	4	13
2	2	1	2	0	0	5
3	0	0	0	0	0	0
4	0	0	0	0	0	0

Technical Document (TD005)

Approved for issue by:

Andrew Gorman
Project Team Physician
AstraZeneca Pharmaceuticals
Alderley Park
Macclesfield, Cheshire
SK10 4TG

Signature.....Date.....

Emma Westhead
Senior Statistician
AstraZeneca Pharmaceuticals
Alderley Park
Macclesfield, Cheshire
SK10 4TG

Signature.....Date.....