

Table 0.1.1
~~Panel 2-2~~

Placebo-Controlled, Double-Blind Studies in the Integrated Summary of Efficacy
 ITT Population

Intent-To-Treat Population	Total (n)	Citalopram Fixed Dose Number of Patients				Citalopram Flexible Dose Number of Patients			Duration of Treatment	Major Efficacy Parameters
		10 mg/day	20 mg/day	40 ^a mg/day	60 ^a mg/day	20-80 mg/day	20-60 mg/day	10-30 mg/day		
I. Short-Term Clinical Studies										
A. Domestic Studies	169									
85A	650	131	130	131	129	129		82	87	Change from Baseline Scores: HAM-D Total Score HAM-D Item 1 MADRS Total Score CGI-S
B. Foreign Studies	200									
89303	274		70	64	66	66			4 Weeks	
89306	149		88	97	89	89			6 Weeks	
86141	142		288	292	284	284		98	6 Weeks	
Subtotal	1442	131	288	292	129	284	82	98	6 Weeks	
II. Longer-Term^b Clinical Studies										
Foreign Studies	226 ^c									
89304	147 ^c		48	57	42	42		152	74	Time to Relapse (MADRS >25;22)
89305 ^d	373		48	57	42	42		152	74	
Subtotal										

^a These groups started at 20 mg/day and ascended within one week to the fixed dose level.

^b All longer-term studies were foreign studies.

^c A total of 391 patients received Citalopram during the initial 8-week, open-label period of the study.

^d Patients in Study 89305 were recruited from short-term, placebo-controlled studies (Studies 89303 and 89306) following response to Citalopram.

^e An additional 60 placebo responders from Studies 89303 and 89306 received continued double-blind placebo in Study 89305.

Note: HAM-D = Hamilton Psychiatric Rating Scale for Depression; MADRS = Montgomery/Asberg Depression Rating Scale; CGI-S = Clinical Global Impression-Severity of Illness.

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23 April 1997

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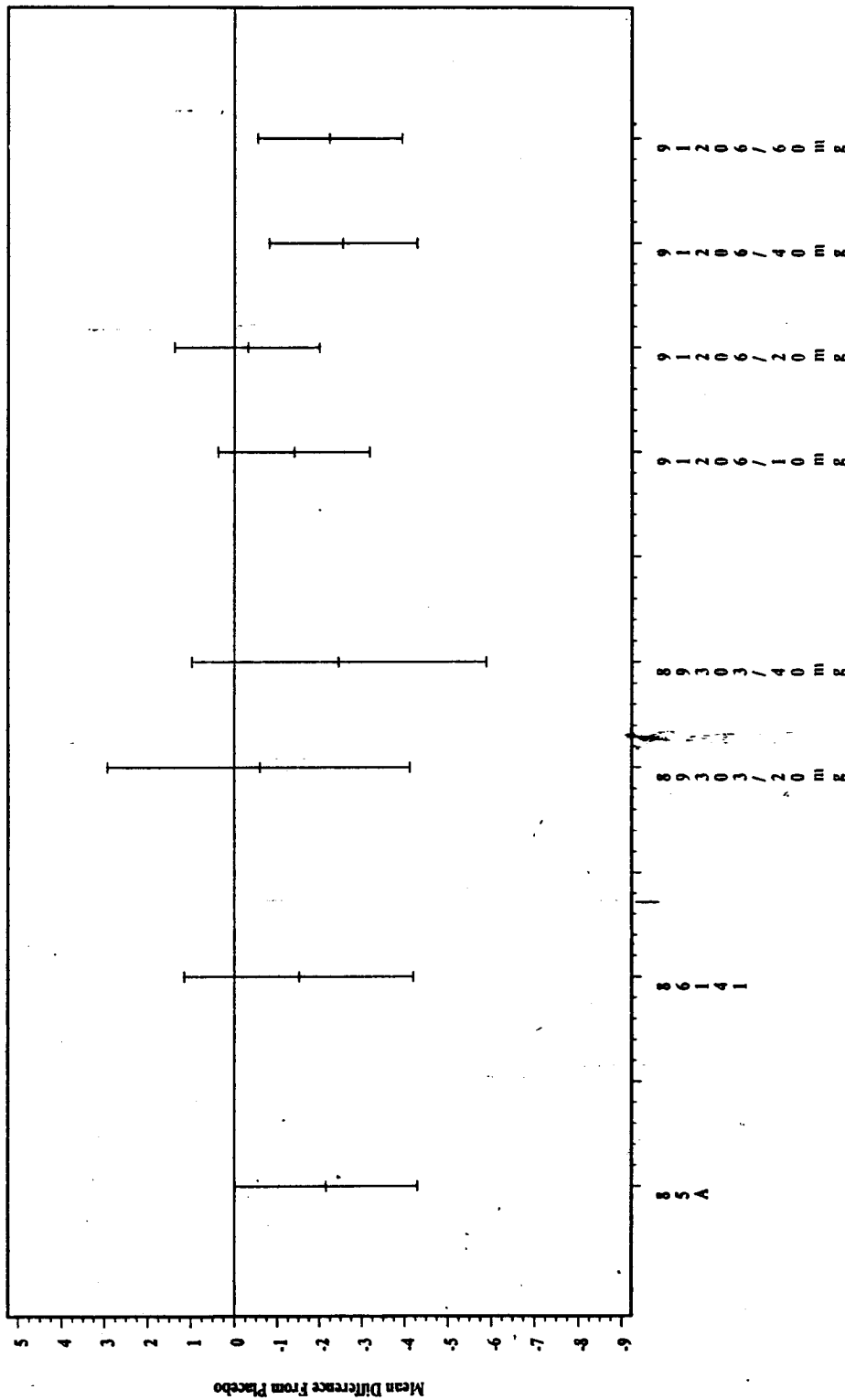
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Figure 0.2.1

Figure 10/02-III-HAMD-1
 Mean Difference Between Citalopram and Placebo with 95% CI
 Using the HAMD 17 Items Total Score Change from Baseline to Endpoint (LOCF)
 Protocol 85A, 91206, 86141 and 89303



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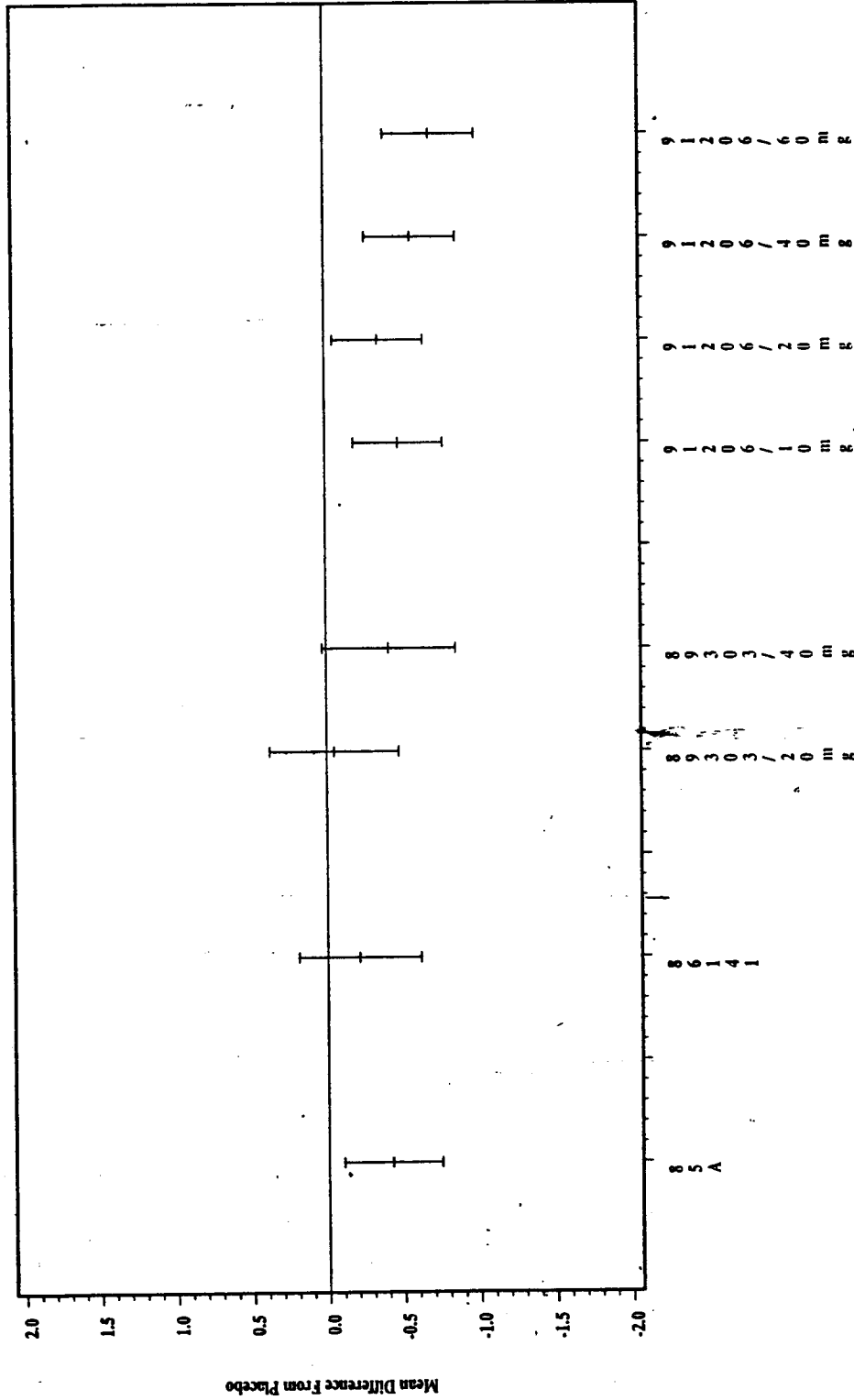
Figure 0.2.2

Figure 10/02-III-MOOD-1

Mean Difference Between Citalopram and Placebo with 95% CI

Using the MOOD Score Change from Baseline to Endpoint (LOCF)

Protocol 85A, 91206, 86141 and 89303

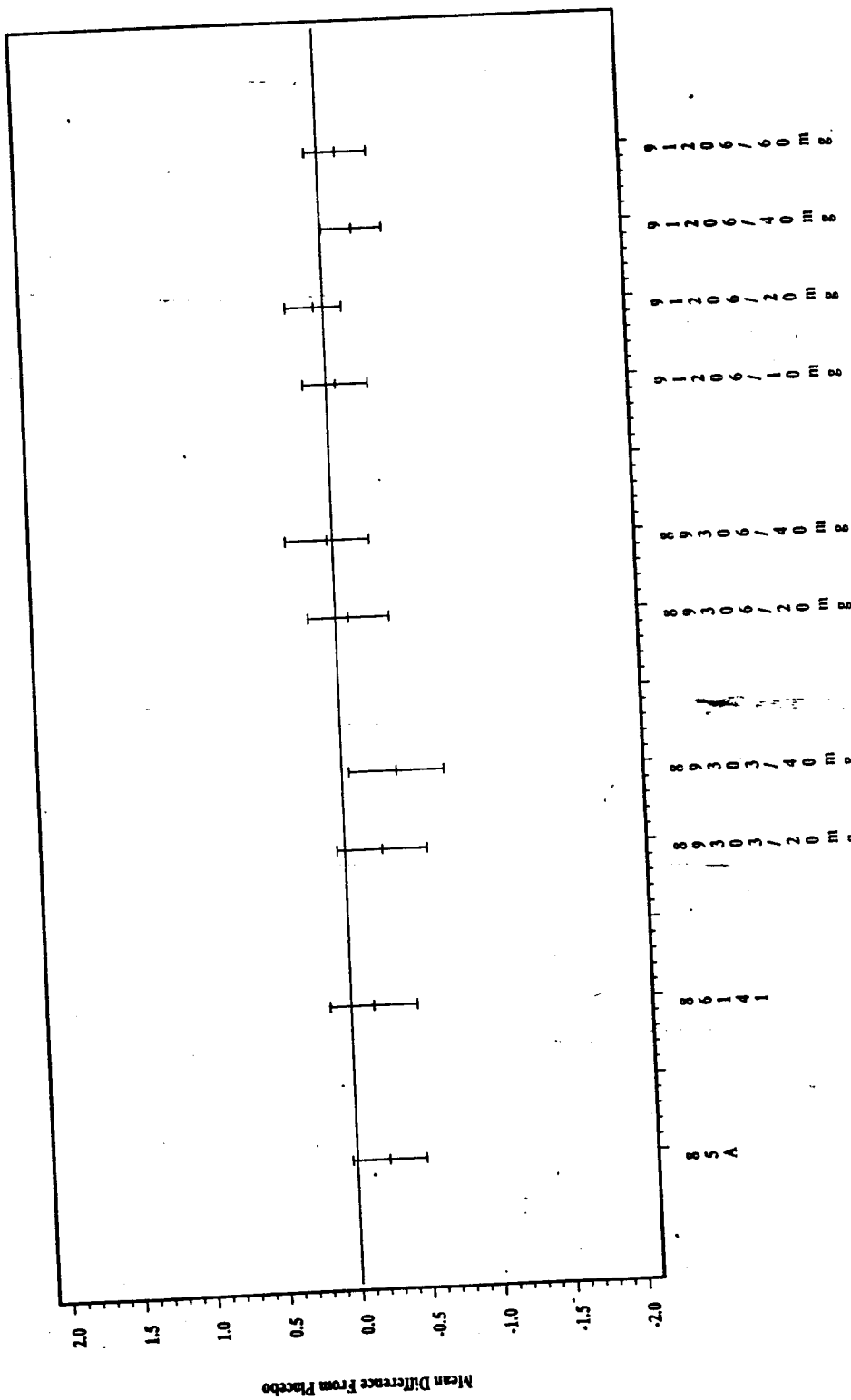


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Figure 0.2.3

Figure 10/02-III-CGIS-1
 Mean Difference Between Citalopram and Placebo with 95% CI
 Using the CGI Severity Score Change from Baseline to Endpoint (LOCF)
 Protocol 85A, 91206, 86141, 89303 and 89306



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0.2.4

Figure 1402444

The 95% CI for Relapse Rate Difference Between Citalopram and Placebo Groups
 Protocols 89304 and 89305

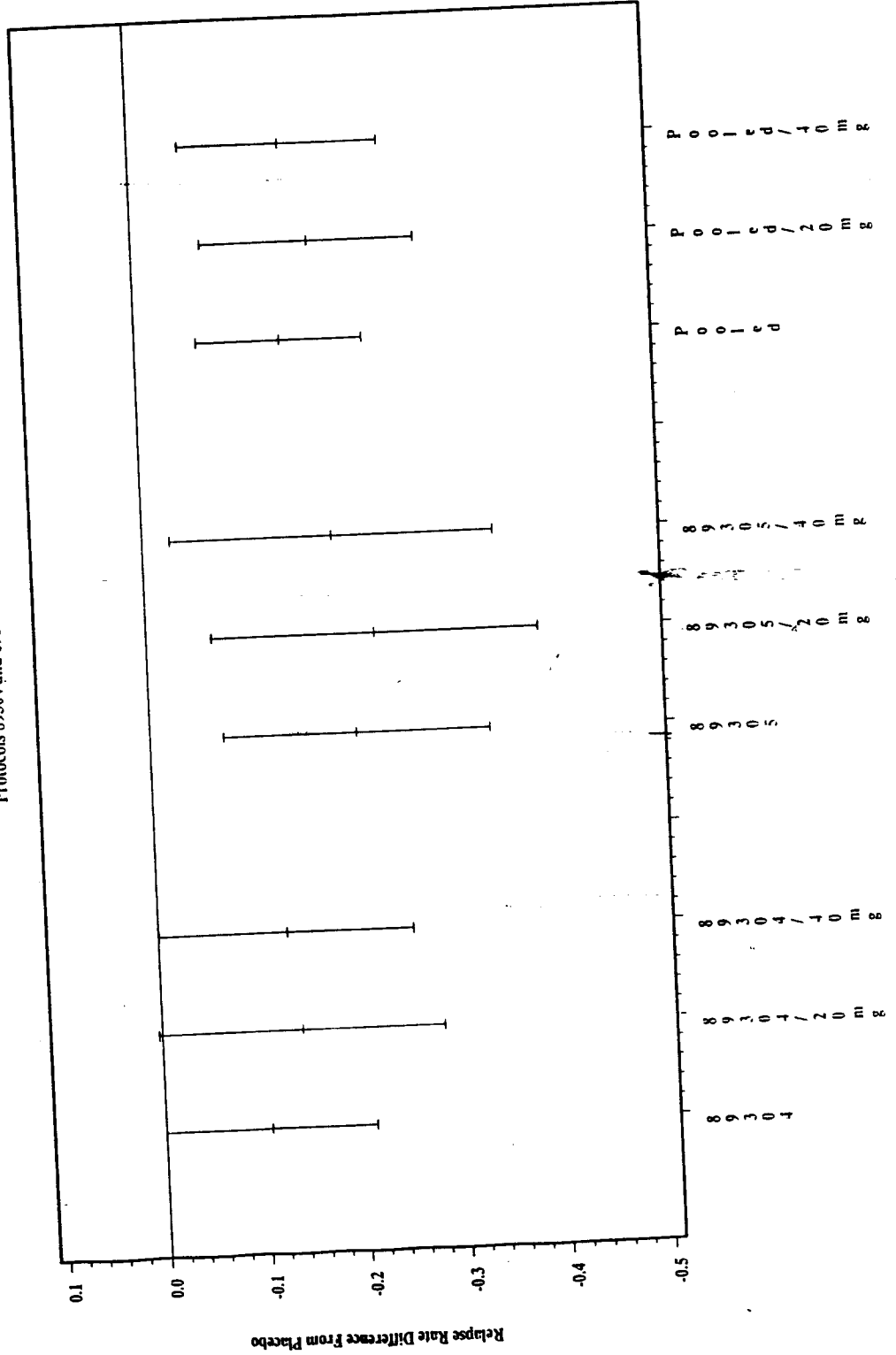


Table 0.3.1

Table 10/02-III-HAMD-2
 Mean Difference Between Citalopram and Placebo
 Using HAMD 17 Items Total Score at Endpoint(LOCF): Protocols 85A, 86141, 89303 and 91206

Study		Dose					
		Placebo	Cital	10 mg	20 mg	40 mg	60 mg
85A (wk 4)	Mean at Baseline	24.13	23.90				
	Mean at Endpoint	17.52	15.11				
	Mean Change at Endpoint	-6.63	-8.78*				
86141 (wk 6)	Mean at Baseline	21.00	22.20				
	Mean at Endpoint	16.10	15.95				
	Mean Change at Endpoint	-4.74	-6.26				
89303 (wk 6)	Mean at Baseline	23.80	24.23	23.17			
	Mean at Endpoint	13.56	13.40	10.48			
	Mean Change at Endpoint	-10.24	-10.83	-12.69			
91206 (wk 6)	Mean at Baseline	21.89	21.67	22.20	21.94	21.64	
	Mean at Endpoint	13.56	13.04	12.47	11.08	11.07	
	Mean Change at Endpoint	-8.32	-8.63	-9.72	-10.87**	-10.56**	
Pooled	Mean at Baseline	22.75	22.44				
	Mean at Endpoint	15.03	12.80				
	Mean Change at Endpoint	-7.70	-9.64**				

*: Significant (p<0.05) when comparing against placebo in mean change at endpoint
 **: Highly significant (p<0.01) when comparing against placebo in mean change at endpoint

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Table 0.3.2

Table 10/02-III-M000-2
 Mean Difference Between Citalopram and Placebo
 Using MOOD Score at Endpoint(LOCF): Protocols 85A, 86141, 89303 and 91206

Study		Dose					
		Placebo	Cital	10 mg	20 mg	40 mg	60 mg
85A (wk 4)	Mean at Baseline	2.70	2.72				
	Mean at Endpoint	1.88	1.46				
	Mean Change at Endpoint	-0.83	-1.26*				
86141 (wk 6)	Mean at Baseline	2.57	2.70				
	Mean at Endpoint	1.88	1.81				
	Mean Change at Endpoint	-0.69	-0.90				
89303 (wk 6)	Mean at Baseline	2.85	2.81		2.81	2.73	
	Mean at Endpoint	1.71	1.63		1.63	1.19	
	Mean Change at Endpoint	-1.14	-1.19		-1.19	-1.55	
91206 (wk 6)	Mean at Baseline	2.84	2.85	2.92	2.85	2.83	2.87
	Mean at Endpoint	1.81	1.47	1.41	1.47	1.23	1.15
	Mean Change at Endpoint	-1.03	-1.38*	-1.51**	-1.38*	-1.60**	-1.73**
Pooled	Mean at Baseline	2.76	2.82				
	Mean at Endpoint	1.82	1.41				
	Mean Change at Endpoint	-0.95	-1.41**				

*: Significant (p<0.05) when comparing against placebo in mean change at endpoint
 **: Highly significant (p<0.01) when comparing against placebo in mean change at endpoint

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Table 0.3.3

Table 10/02-111-CGIS-2
 Mean Difference Between Citalopram and Placebo
 Using CGI Severity Score at Endpoint (LOCF): Protocols 85A, 86141, 89303, 89306 and 91026

Study		Dose					
		Placebo	Cital	10 mg	20 mg	40 mg	60 mg
85A (wk 4)	Mean at Baseline	3.60	3.60				
	Mean at Endpoint	2.93	2.70				
	Mean Change at Endpoint	-0.67	-0.90*				
86141 (wk 6)	Mean at Baseline	3.10	3.22				
	Mean at Endpoint	2.71	2.67				
	Mean Change at Endpoint	-0.39	-0.55				
89303 (wk 6)	Mean at Baseline	3.30	3.39	3.30	3.30	3.30	
	Mean at Endpoint	2.61	2.43	2.43	2.22	2.22	
	Mean Change at Endpoint	-0.70	-0.96	-0.96	-1.08*	-1.08*	
89306 (wk 6)	Mean at Baseline	3.30	3.28	3.28	3.28	3.22	
	Mean at Endpoint	2.36	2.25	2.31	2.20	2.22	
	Mean Change at Endpoint	-0.94	-1.03	-0.91	-1.09*	-1.00	
91206 (wk 6)	Mean at Baseline	3.27	3.28	3.28	3.28	3.22	
	Mean at Endpoint	2.40	2.35	2.35	2.40	2.22	
	Mean Change at Endpoint	-0.87	-0.93	-0.93	-0.80	-1.00	
Pooled	Mean at Baseline	3.33	3.29				
	Mean at Endpoint	2.57	2.37				
	Mean Change at Endpoint	-0.76	-0.92**				

not significant by multiple comparison adjustment.

*: Significant (p<0.05) when comparing against placebo in mean change at endpoint
 **: Highly significant (p<0.01) when comparing against placebo in mean change at endpoint

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0.3-4

Table 10.3-4
Summary of Patients Who Relapsed, In the Placebo-Controlled
Long-Term Studies
ITT Population

Study and Treatment Group	Crude Relapse Rate n(%)	P-value of Citalopram vs. Placebo for Time to Relapse
Study 89304		
Citalopram up to 60 mg (n=152)	21(14%)	0.044 *
Citalopram 20 mg (n=48)	5(10%)	0.066
Citalopram 40 mg (n=69)	8(12%)	0.044 *
Placebo (n=74)	18(24%)	
Study 89305		
Citalopram 20-40 mg (n=105)	11(10%)	0.002 **
Citalopram 20 mg (n=48)	4(8%)	0.006 **
Citalopram 40 mg (n=57)	7(12%)	0.022 *
Placebo (n=42)	13(31%)	
Pooled		
Citalopram up to 60 mg (n=257)	32(12%)	0.001 **
Citalopram 20 mg (n=96)	9(9%)	0.002 **
Citalopram 40 mg (n=126)	15(12%)	0.003 **
Placebo (n=116)	31(27%)	

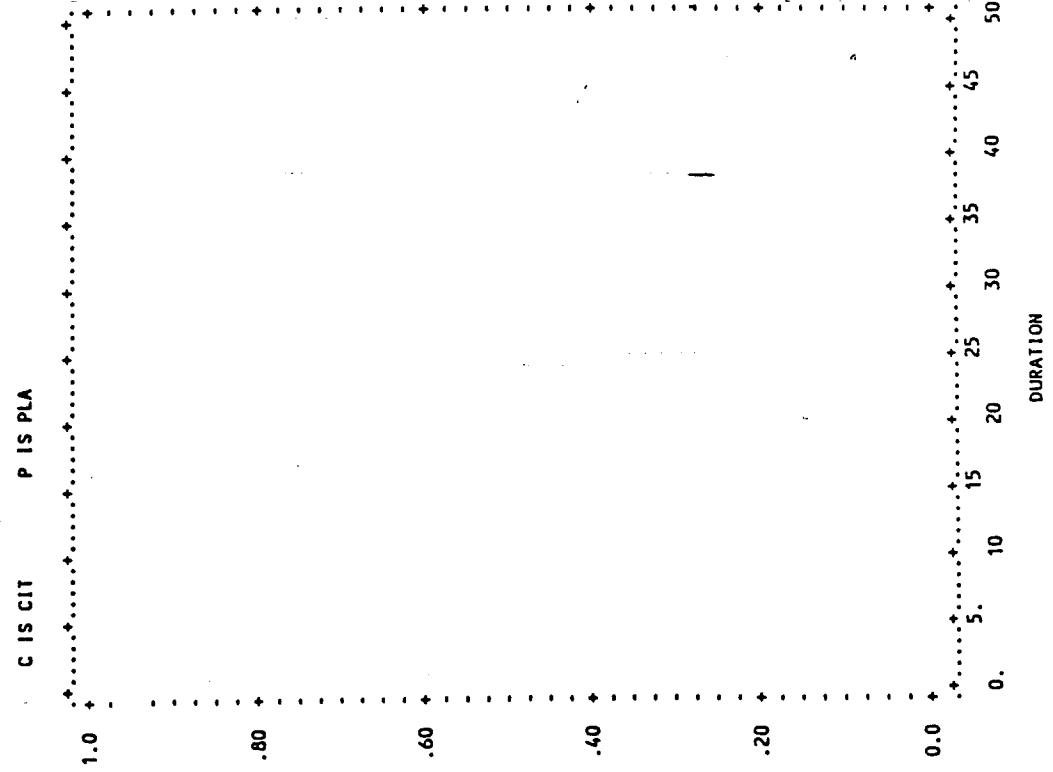
*: P-value ≤ 0.05, **: P-value ≤ 0.01.
 The P-value are from the log-rank test in the LIFETEST procedure of SAS.
 Relapse = MADRS ≥ 25 for Study 89304; MADRS ≥ 22 for Study 89305 as defined in the NDA.
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Figure 1.2.1.

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PAGE 7 BMDP1L PREMATURE TERMINATION DUE TO LACK OF EFFECT: STUDY 85A
CUMULATIVE PROPORTION SURVIVING GROUP VAR: TRI



PAGE 14 BMDP1L PREMATURE TERMINATION FOR ALL REASONS: STUDY 85A
CUMULATIVE PROPORTION SURVIVING GROUP VAR: TRI



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1.3.1
Table 07/03-1

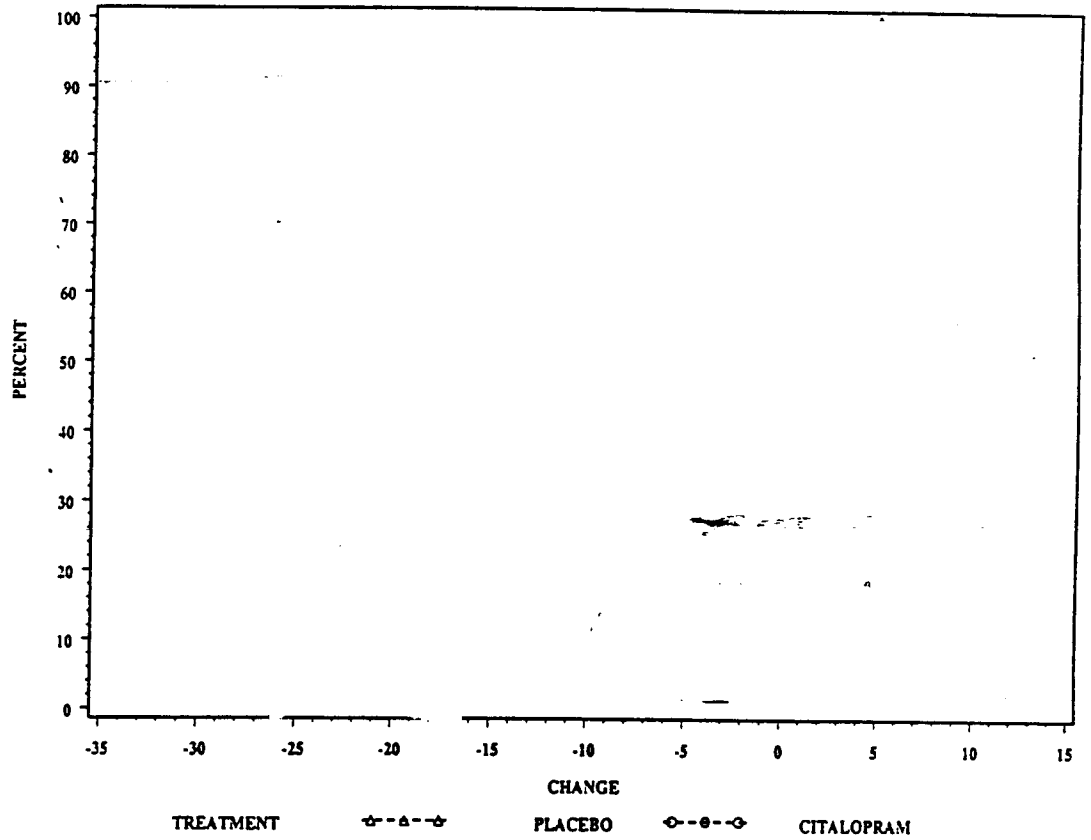
Study: 85A													
Least Square Mean Change from Baseline in HAM-D 24-Item Total Score													
LAST OBSERVATION CARRIED FORWARD ANALYSIS													
Treatment Groups	Baseline LS Mean		Treatment Week				Treatment Week						
	n*	X	Week1	Week2	Week3	Week4	Week1	Week2	Week3	Week4			
CITALOPRAM	78	33.52	78	-6.42	78	-10.43	78	-12.04	78	-12.90	78	-12.90	
PLACEBO	82	33.72	82	-3.95	82	-6.66	82	-9.18	82	-9.58	82	-9.58	
2-sided p-values for treatment effect													
CIT vs PLAC	0.7766		0.0116				0.0027				0.0565		0.0344
OBSERVED CASES ANALYSIS													
Treatment Groups	Baseline LS Mean		Treatment Week				Treatment Week						
	n*	X	Week1	Week2	Week3	Week4	Week1	Week2	Week3	Week4			
CITALOPRAM	78	33.52	75	-6.75	62	-12.42	62	-15.47	43	-18.29	43	-18.29	
PLACEBO	82	33.72	79	-4.13	69	-6.70	69	-11.25	42	-14.11	42	-14.11	
2-sided p-values for treatment effect													
CIT vs PLAC	0.7766		0.0086				0.0001				0.0159		0.0250

* There are 4 subjects with missing HAM-D 24-item total score in base line in the Citalopram group and 5 subjects in the placebo group. These subjects were not included in the analysis of HAM-D 24-item total score.

CITALOPRAM PROTOCOL: 85A

1.3.2
FIGURE (11)

CHANGE IN HAMD BASELINE TO LOCF

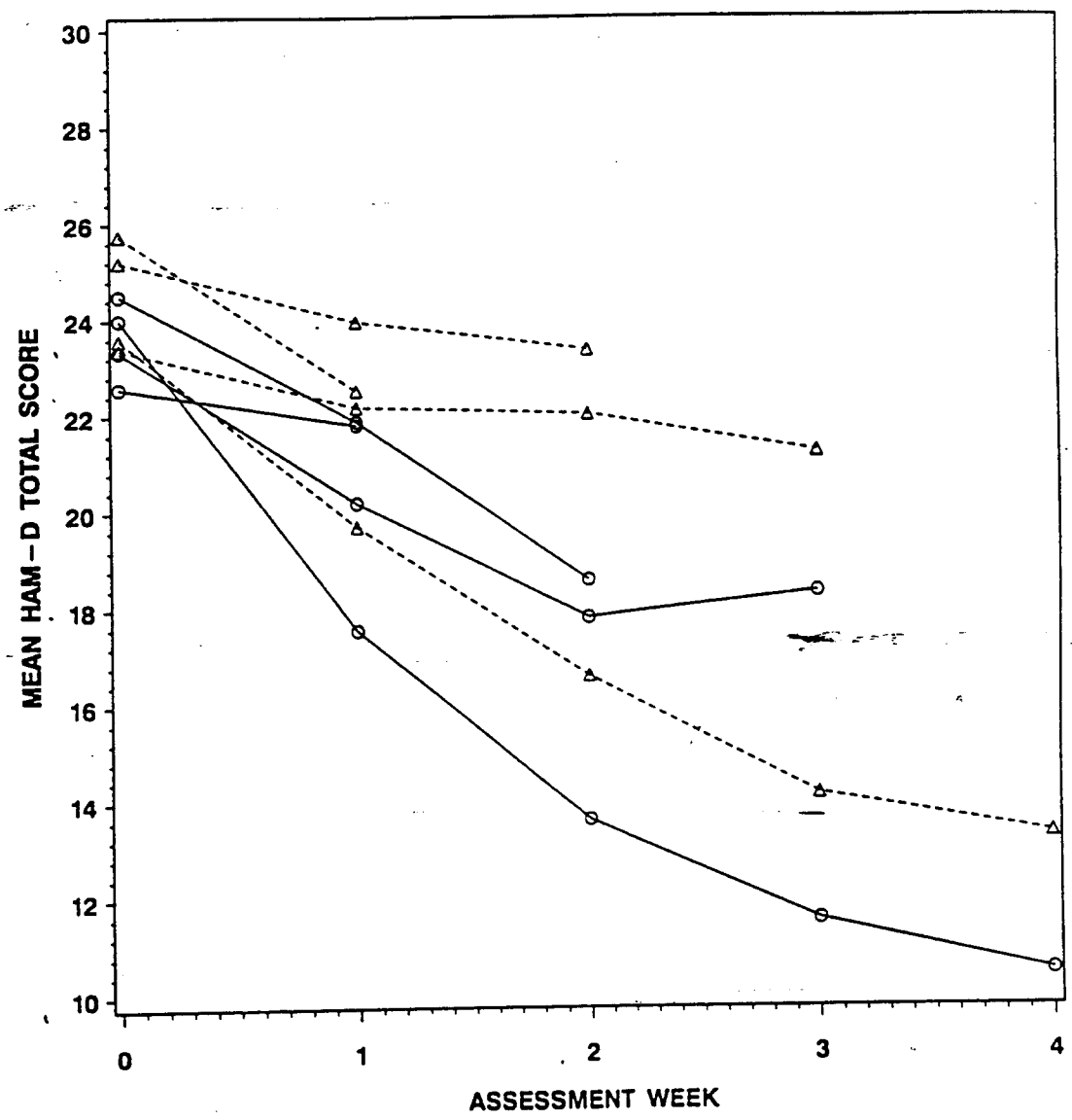


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CITALOPRAM PROTOCOL: 85A

FIGURE ~~2~~ 1.3.3
HAM-D TOTAL SCORE



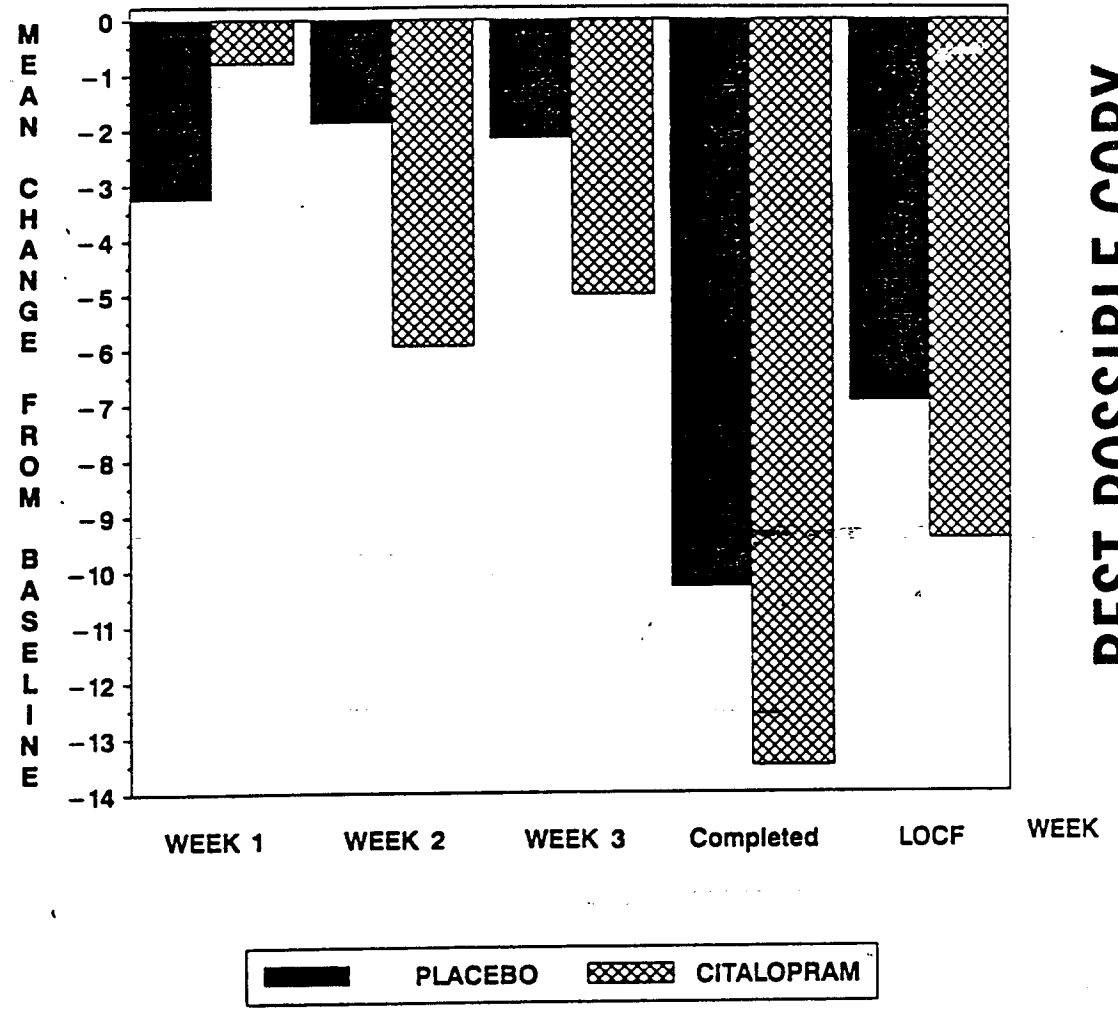
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Triangle: Placebo Circle: Citalopram

Plot generated by program fig2_85a.sas (10FEB97)

CITALOPRAM PROTOCOL: 85A

FIGURE 1.3. 4
HAMD TOTAL SCORE
AT THE TIME OF DROPOUT, AND COMPLETERS



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Plot generated by program flg3_85a.sas (10FEB97)

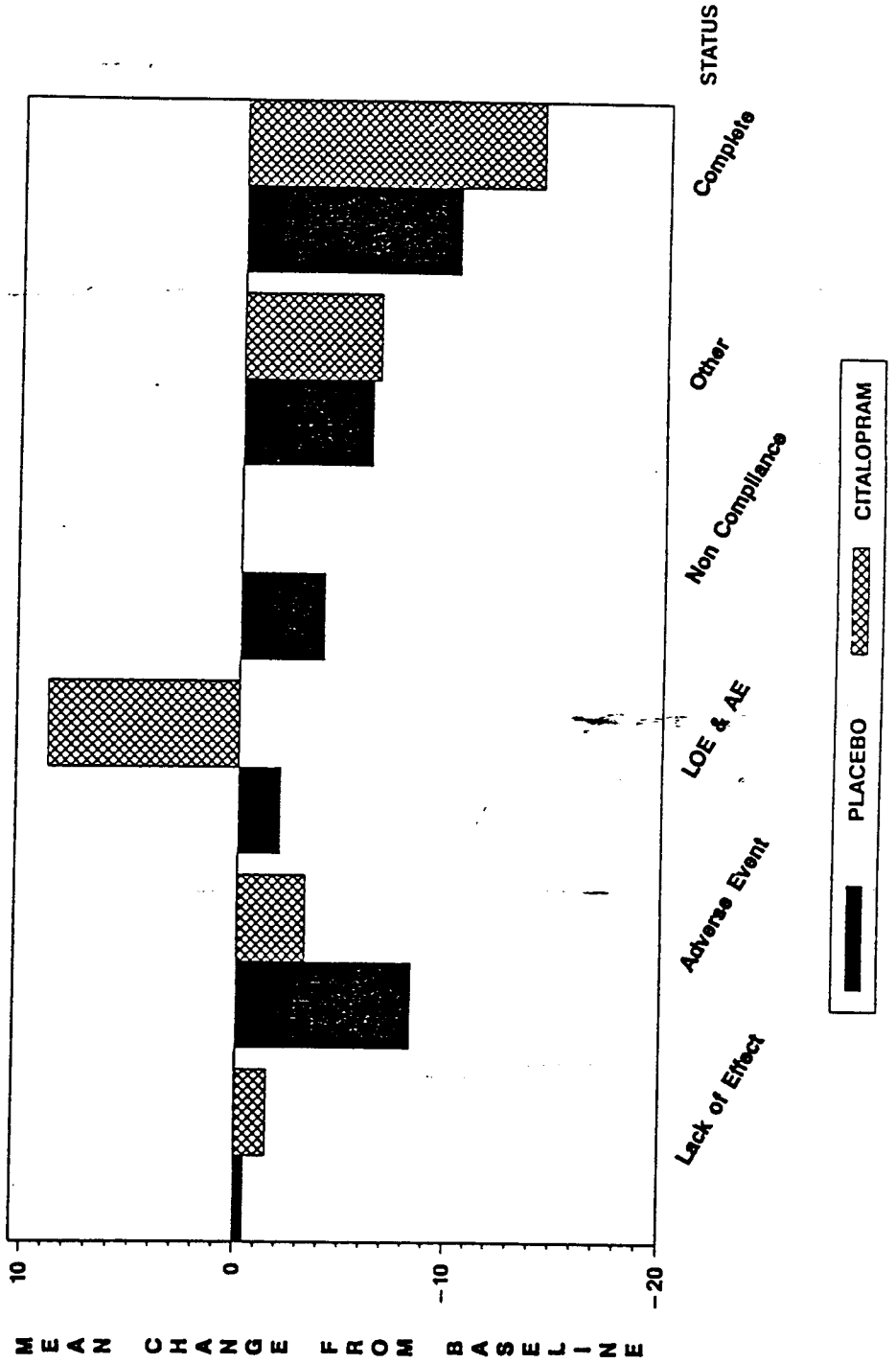
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CITALOPRAM PROTOCOL: 85A

FIGURE 4 ~~4~~ 1.3.5
HAMD TOTAL SCORE
BY WITHDRAWAL REASON, TOGETHER WITH COMPLETERS



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1.4.1

Table 07/03-LS

Study: 85A												
Least Square Mean Change from Baseline in HAM-D Depressed Mood Item												
LAST OBSERVATION CARRIED FORWARD ANALYSIS												
Treatment Groups	Treatment Week											
	Baseline LS Mean		Week1		Week2		Week3		Week4			
	n	X	n	Δ	n	Δ	n	Δ	n	Δ		
CITALOPRAM	82	2.68	82	-0.68	82	-1.06	82	-1.19	82	-1.34		
PLACEBO	87	2.71	87	-0.35	87	-0.64	87	-0.85	87	-0.85		
2-sided p-values for treatment effect												
CIT vs PLAC	0.7856		0.0044		0.0021		0.0234		0.0023			
OBSERVED CASES ANALYSIS												
Treatment Groups	Treatment Week											
	Baseline LS Mean		Week1		Week2		Week3		Week4			
	n	X	n	Δ	n	Δ	n	Δ	n	Δ		
CITALOPRAM	82	2.68	80	-0.70	66	-1.17	53	-1.45	48	-1.84		
PLACEBO	87	2.71	86	-0.35	75	-0.67	62	-1.06	50	-1.29		
2-sided p-values for treatment effect												
CIT vs PLAC	0.7856		0.0026		0.0006		0.0240		0.0024			

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1.5.1
Table 07403-1-6

Study: 85A													
Least Square Mean Change from Baseline in CGI-Severity Score													
LAST OBSERVATION CARRIED FORWARD ANALYSIS													
Treatment Groups	Baseline LS Mean		Treatment Week				Treatment Week				Treatment Week		
	n*	X	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	
CITALOPRAM	81	3.61	81	-0.38	81	-0.74	81	-0.87	81	-0.87	81	-0.94	
PLACEBO	87	3.61	87	-0.23	87	-0.40	87	-0.63	87	-0.63	87	-0.68	
2-sided p-values for treatment effect													
CIT vs PLAC	0.9841		0.0824				0.0024				0.0650		0.0508
OBSERVED CASES ANALYSIS													
Treatment Groups	Baseline LS Mean		Treatment Week				Treatment Week				Treatment Week		
	n*	X	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	
CITALOPRAM	81	3.61	79	-0.39	63	-0.92	51	-1.09	47	-1.09	47	-1.32	
PLACEBO	87	3.61	85	-0.23	75	-0.40	61	-0.81	51	-0.81	51	-0.98	
2-sided p-values for treatment effect													
CIT vs PLAC	0.9841		0.0734				0.0001				0.0645		0.0373

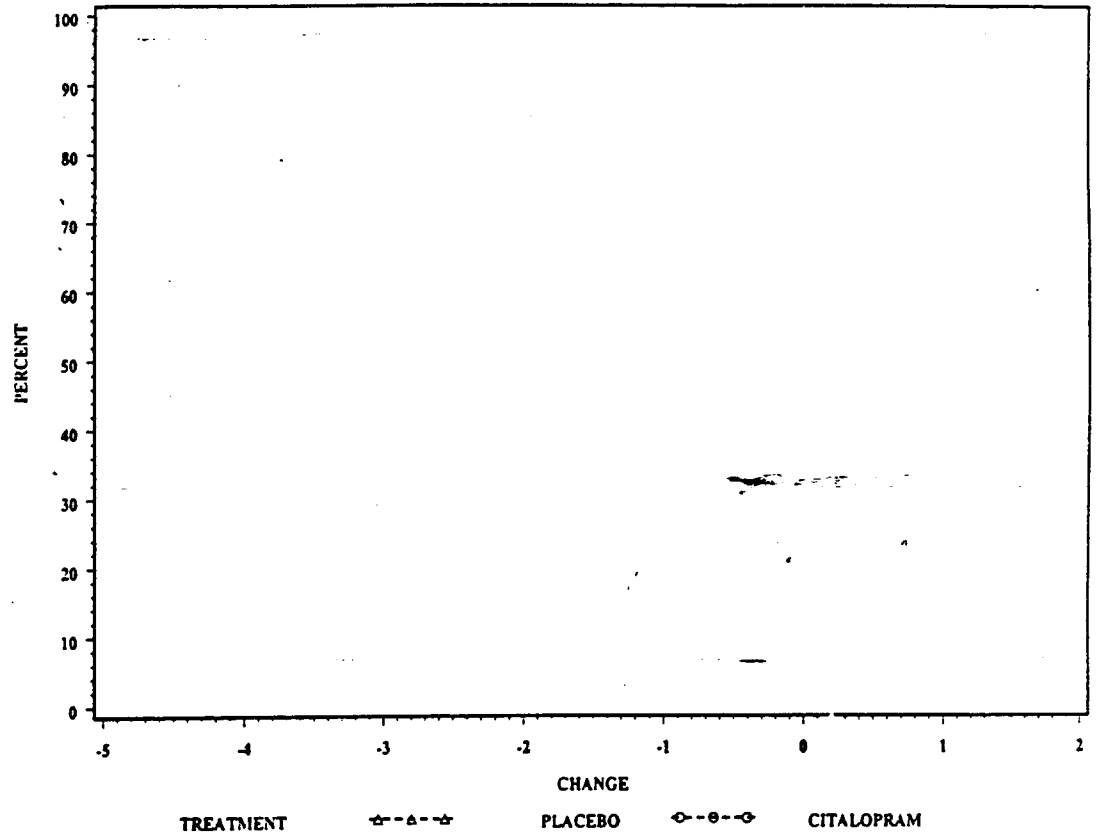
* There is 1 subject with missing CGI severity of illness score in baseline in the Citalopram group. That patient was not included in the analysis of CGI severity of illness score.

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CITALOPRAM PROTOCOL: 85A

1.5.2
FIGURE ~~(1.2)~~

CHANGE IN CGI-S BASELINE TO LOCF



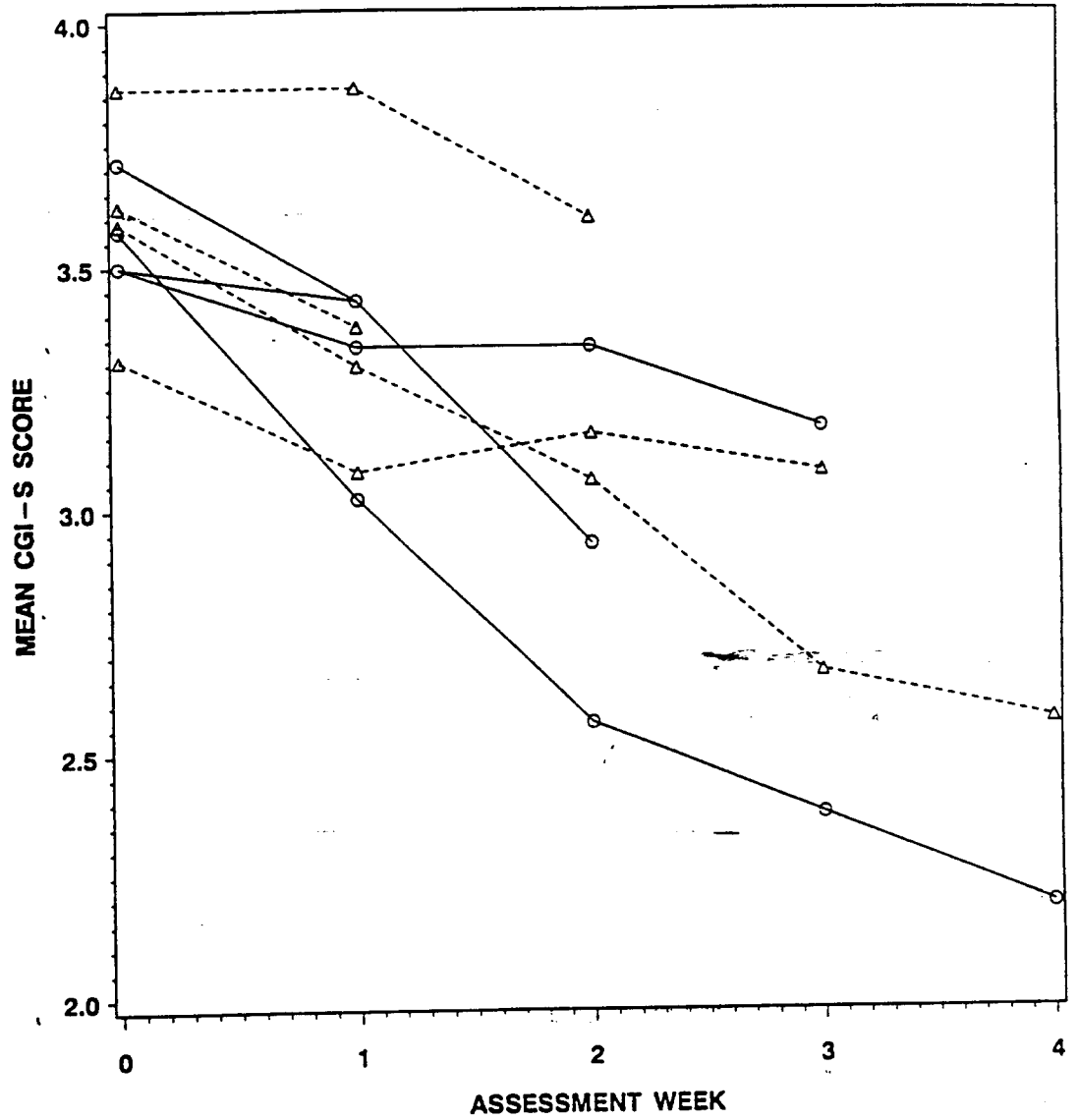
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CITALOPRAM PROTOCOL: 85A

1.5.3

FIGURE ~~2-2~~

CGI SEVERITY OF ILLNESS SCORE

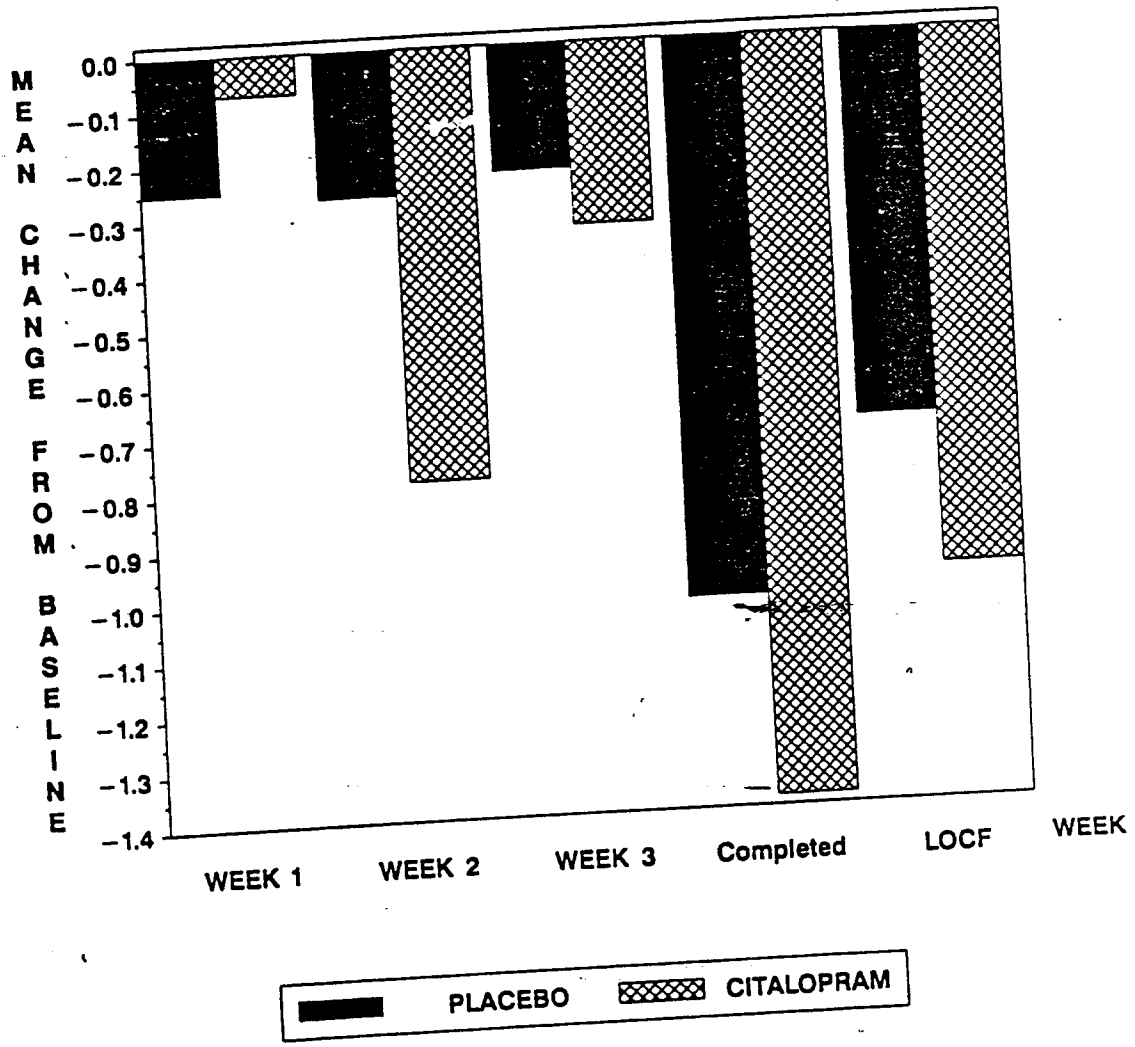


Triangle: Placebo Circle: Citalopram

Plot generated by program fig2_85a.sas (10FEB97)

CITALOPRAM PROTOCOL: 85A

FIGURE ~~3.2~~^{1.5-4}
CGI SEVERITY OF ILLNESS SCORE
AT THE TIME OF DROPOUT, AND COMPLETERS



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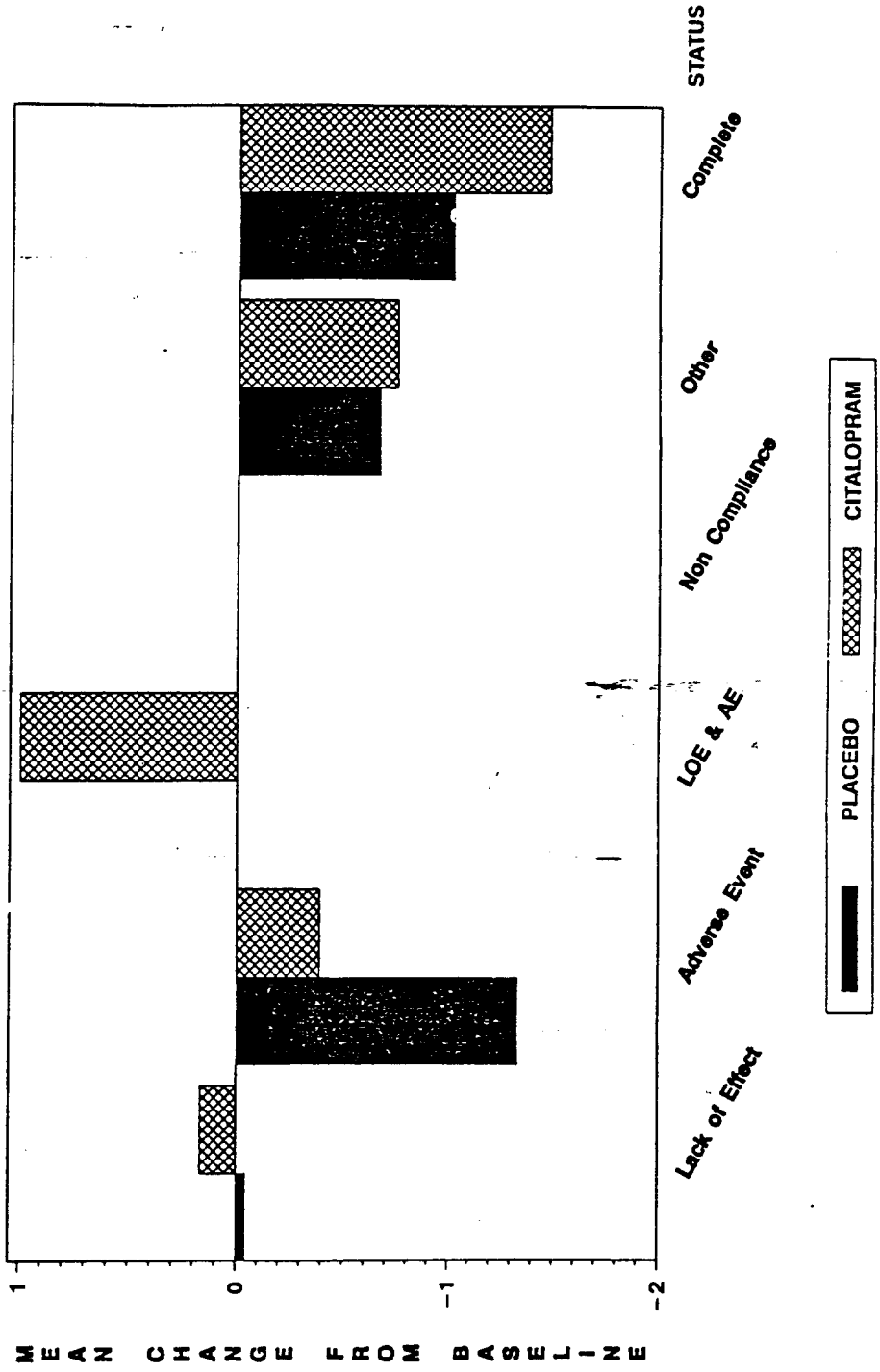
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CITALOPRAM PROTOCOL: 85A

FIGURE 2 *1:5.5*
CGI SEVERITY OF ILLNESS SCORE
BY WITHDRAWAL REASON, TOGETHER WITH COMPLETERS



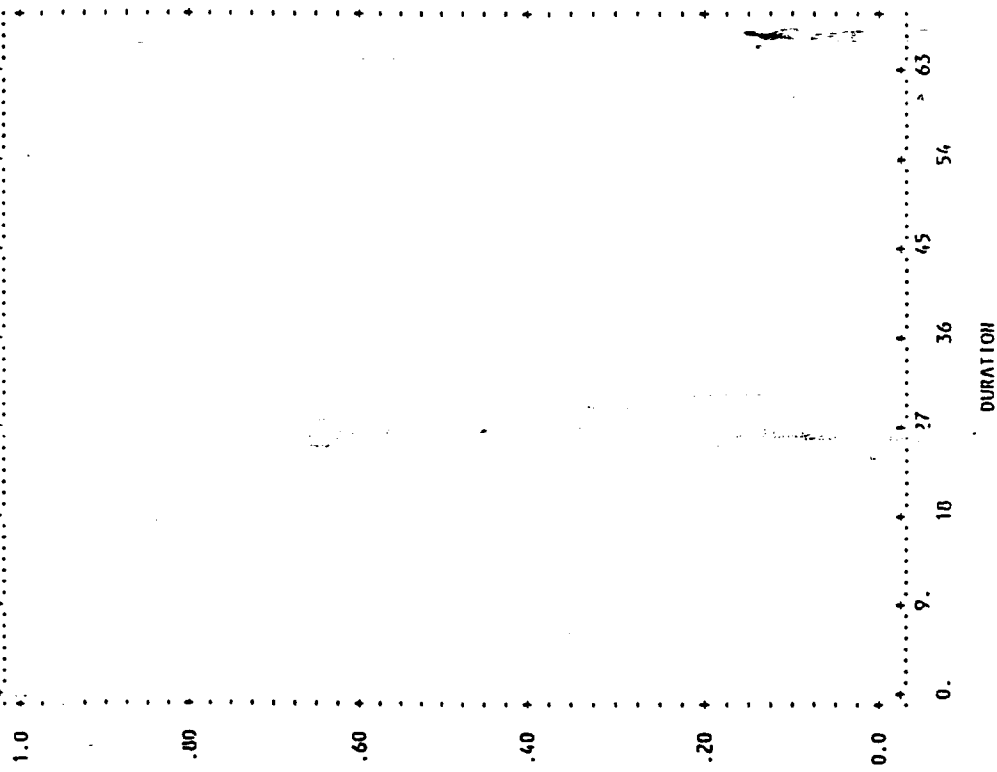
Plot generated by program fig4_141.sas (10FEB97)

Figure 2.2.1

PAGE 166 UMDP1L PREMATURE TERMINATION FOR ALL REASONS: STUDY 91206

CUMULATIVE PROPORTION SURVIVING GROUP VAR: TRTZ

A IS CIT_10mg B IS CIT_20mg C IS CIT_40mg D IS CIT_60mg
E IS PLA

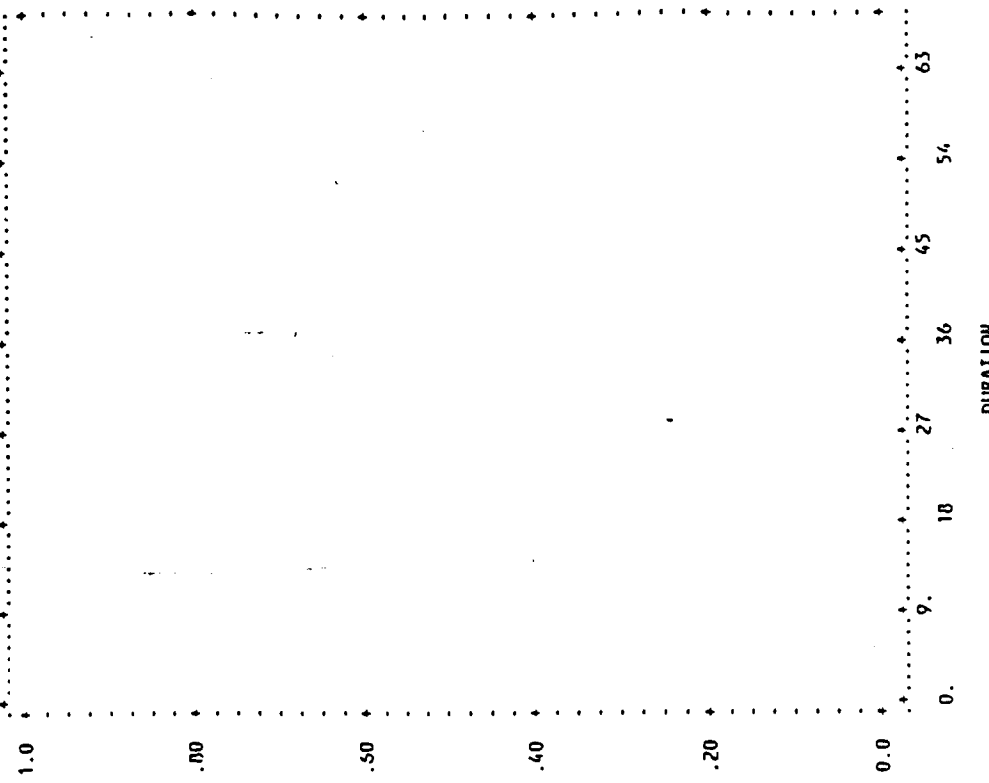


NUMBER OF INTEGER WORDS OF STORAGE USED IN PRECEDING PROBLEM 4906
CPU TIME USED 0.070 SECONDS

PAGE 140 UMDP1L PREMATURE TERMINATION DUE TO LACK OF EFFECT: STUDY 91206

CUMULATIVE PROPORTION SURVIVING

A IS CIT_10mg B IS CIT_20mg C IS CIT_40mg D IS CIT_60mg
E IS PLA



NUMBER OF INTEGER WORDS OF STORAGE USED IN PRECEDING PROBLEM 4754
CPU TIME USED 0.300 SECONDS

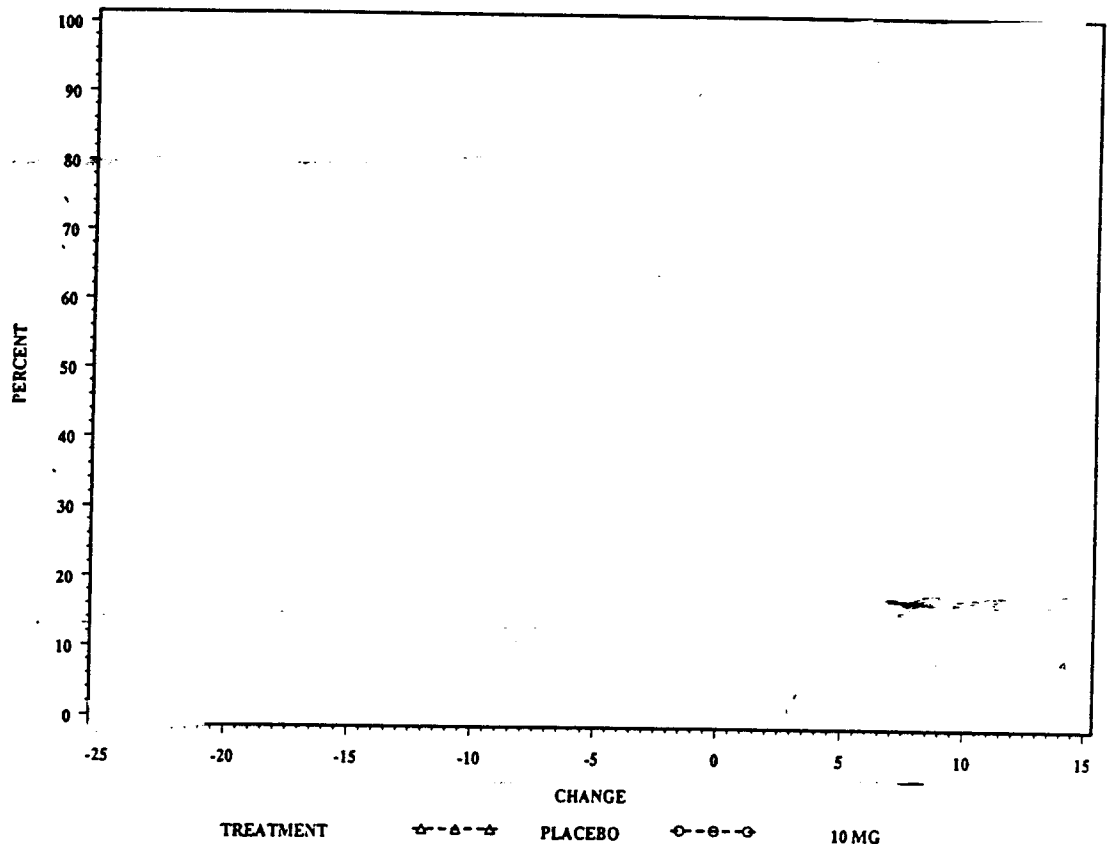
Table ~~02022229~~ 2.3.1

Treatment Groups		Least Square Mean Change from Baseline in HAM-D 21-item Total Score																											
		LAST OBSERVATION CARRIED FORWARD ANALYSIS																											
		Baseline LS Mean						Week1				Week2				Week3				Week4				Week5				Week6	
n	x	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ				
CIT 10mg	123	24.98	-4.41	123	-7.24	123	-8.66	123	-9.64	123	-10.42	123	-10.78	123	-10.42	123	-9.64	123	-8.66	123	-7.24	123	-4.41	123	24.98				
CIT 20mg	128	24.24	-4.11	128	-6.19	128	-8.08	128	-8.85	128	-9.60	128	-9.94	128	-9.60	128	-8.85	128	-8.08	128	-6.19	128	-4.11	128	24.24				
CIT 40mg	120	24.44	-4.27	120	-6.89	120	-9.34	120	-10.19	120	-11.34	120	-12.22	120	-11.34	120	-10.19	120	-9.34	120	-6.89	120	-4.27	120	24.44				
CIT 60mg	110	24.52	-4.22	110	-6.22	110	-8.76	110	-10.34	110	-11.15	110	-12.05	110	-11.15	110	-10.34	110	-8.76	110	-6.22	110	-4.22	110	24.52				
PLACEBO	124	24.62	-4.20	124	-6.44	124	-8.36	124	-8.65	124	-9.20	124	-9.31	124	-9.20	124	-8.65	124	-8.36	124	-6.44	124	-4.20	124	24.62				
2-sided p-values for pairwise comparisons from contrast																													
10mg vs PLAC	0.3661	0.7181	0.2612	0.7117	0.2459	0.1875	0.1238																						
20mg vs PLAC	0.3498	0.8904	0.7186	0.7333	0.8165	0.6631	0.5064																						
40mg vs PLAC	0.6584	0.8962	0.5281	0.2309	0.0740	0.0223	0.0025																						
60mg vs PLAC	0.8163	0.8866	0.7174	0.6345	0.0549	0.0415	0.0053																						
OBSERVED CASES ANALYSIS																													
Treatment Groups		Least Square Mean Change from Baseline in HAM-D 21-item Total Score																											
		LAST OBSERVATION CARRIED FORWARD ANALYSIS																											
		Baseline LS Mean						Week1				Week2				Week3				Week4				Week5				Week6	
n	x	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ				
CIT 10mg	123	24.98	-4.42	116	-7.44	106	-9.51	101	-10.97	92	-12.86	89	-13.16	92	-12.86	92	-10.76	92	-9.38	104	-9.38	100	-11.24	86	-13.90				
CIT 20mg	128	24.24	-4.14	113	-6.21	104	-8.48	104	-9.38	92	-10.76	87	-11.30	92	-10.76	92	-9.38	104	-9.38	100	-11.24	86	-13.90	76	-13.52				
CIT 40mg	120	24.44	-4.33	108	-7.31	107	-9.87	100	-11.24	94	-12.79	86	-13.90	94	-12.79	94	-10.76	94	-9.38	100	-11.24	86	-13.90	76	-13.52				
CIT 60mg	110	24.52	-4.22	100	-6.54	95	-9.21	90	-10.78	80	-12.15	76	-13.52	90	-12.15	80	-10.78	80	-9.21	90	-10.78	80	-12.15	76	-13.52				
PLACEBO	124	24.62	-4.34	117	-6.54	112	-8.61	104	-9.38	92	-10.99	85	-11.91	104	-9.38	92	-10.99	92	-8.61	104	-9.38	92	-10.99	85	-11.91				
2-sided p-values for pairwise comparisons from contrast																													
10mg vs PLAC	0.3661	0.8979	0.2148	0.2837	0.0749	0.0564	0.2129																						
20mg vs PLAC	0.3498	0.7323	0.6581	0.8849	0.9940	0.8169	0.5456																						
40mg vs PLAC	0.6584	0.9821	0.2981	0.1325	0.0368	0.0658	0.0504																						
60mg vs PLAC	0.8163	0.8376	0.9983	0.4875	0.1262	0.2552	0.1261																						

CITALOPRAM PROTOCOL: 91206

FIGURE ~~(1-2-1)~~ 2.3.2a

CHANGE IN HAMD BASELINE TO LOCF



Plot generated by program fig1_206.sas (10FEB97)

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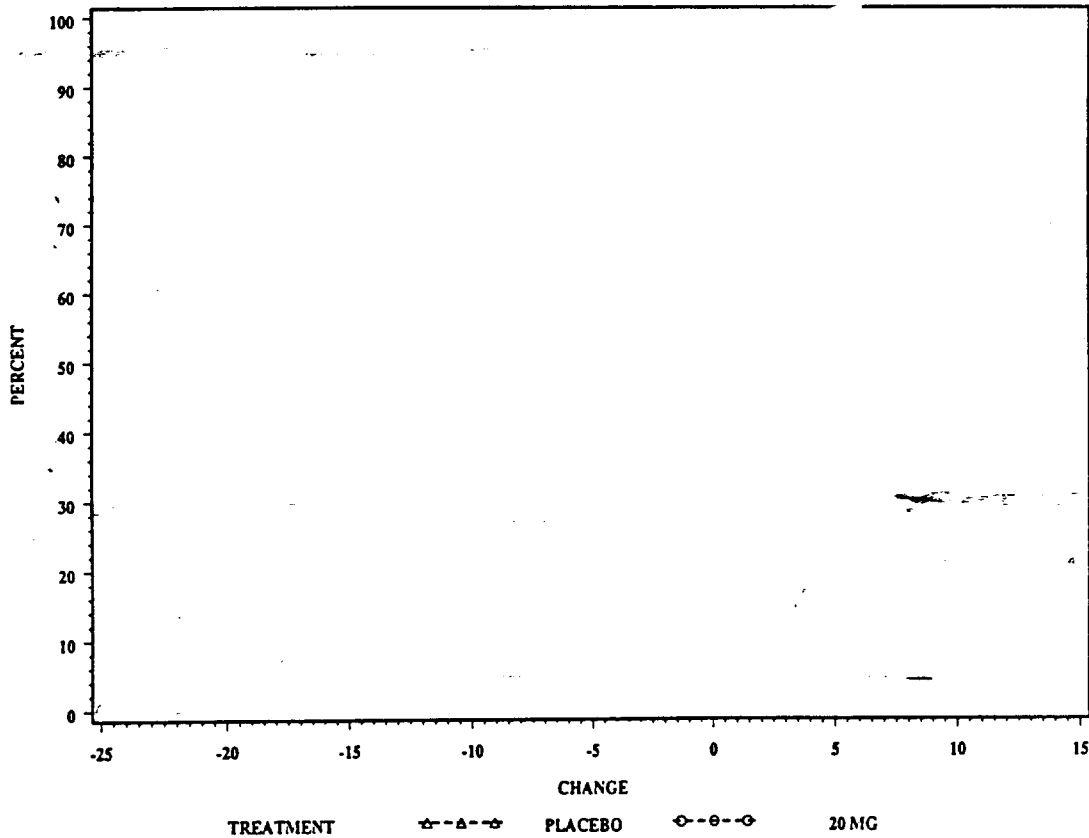
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CITALOPRAM PROTOCOL: 91206

FIGURE (1-2-2) 2.3.26

CHANGE IN HAMD BASELINE TO LOCF

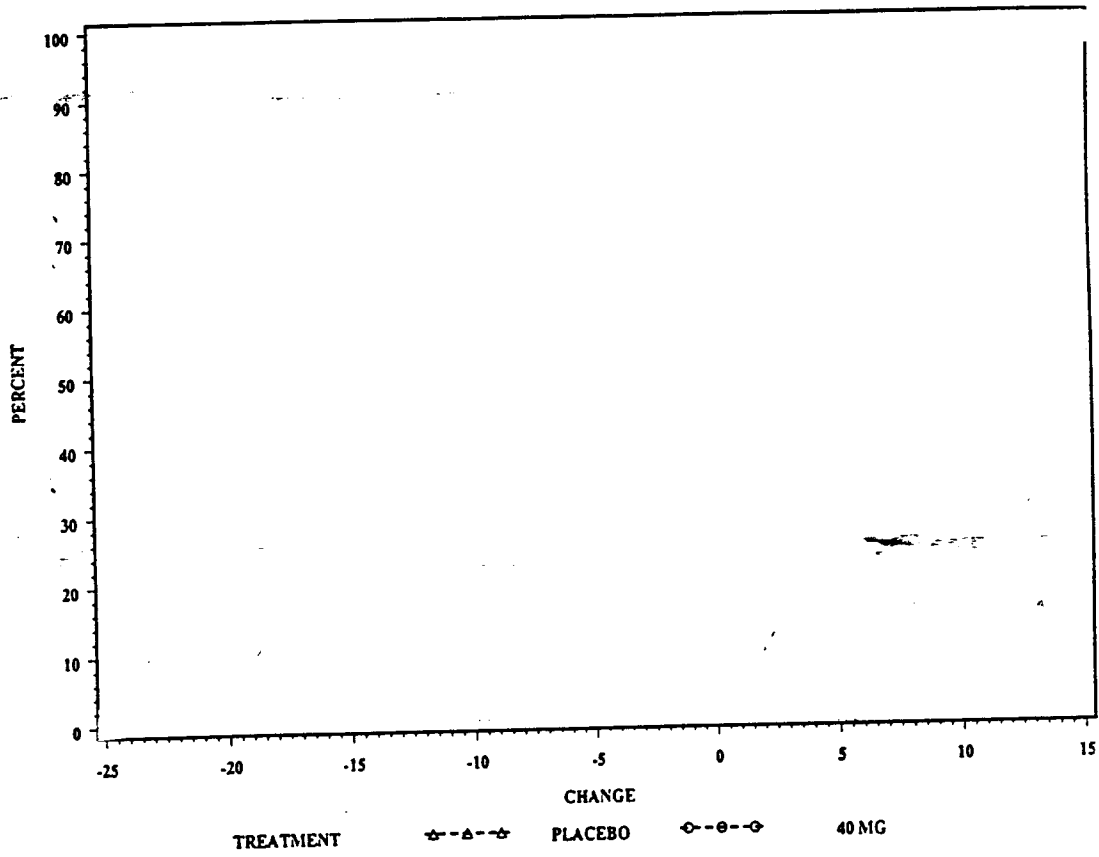


Plot generated by program fig1_206.sas (10FEB97)

CITALOPRAM PROTOCOL: 91206 ...

FIGURE ~~(1-2-3)~~ 2.3.2c

CHANGE IN HAMD BASELINE TO LOCF



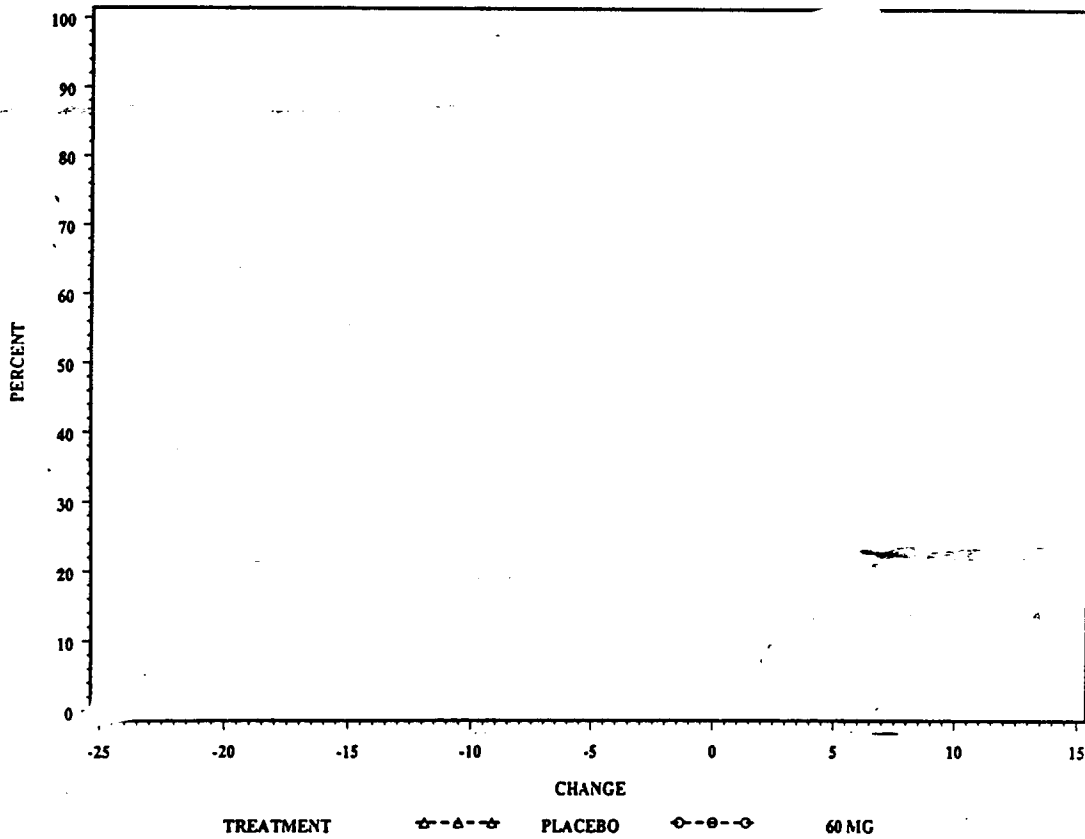
Plot generated by program fig1_206.sas (10FEB97)

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CITALOPRAM PROTOCOL: 91206

FIGURE ~~(1-2-4)~~ 2-3. 2 cl

CHANGE IN HAMD BASELINE TO LOCF



Plot generated by program fig1_206.sas (10FEB97)

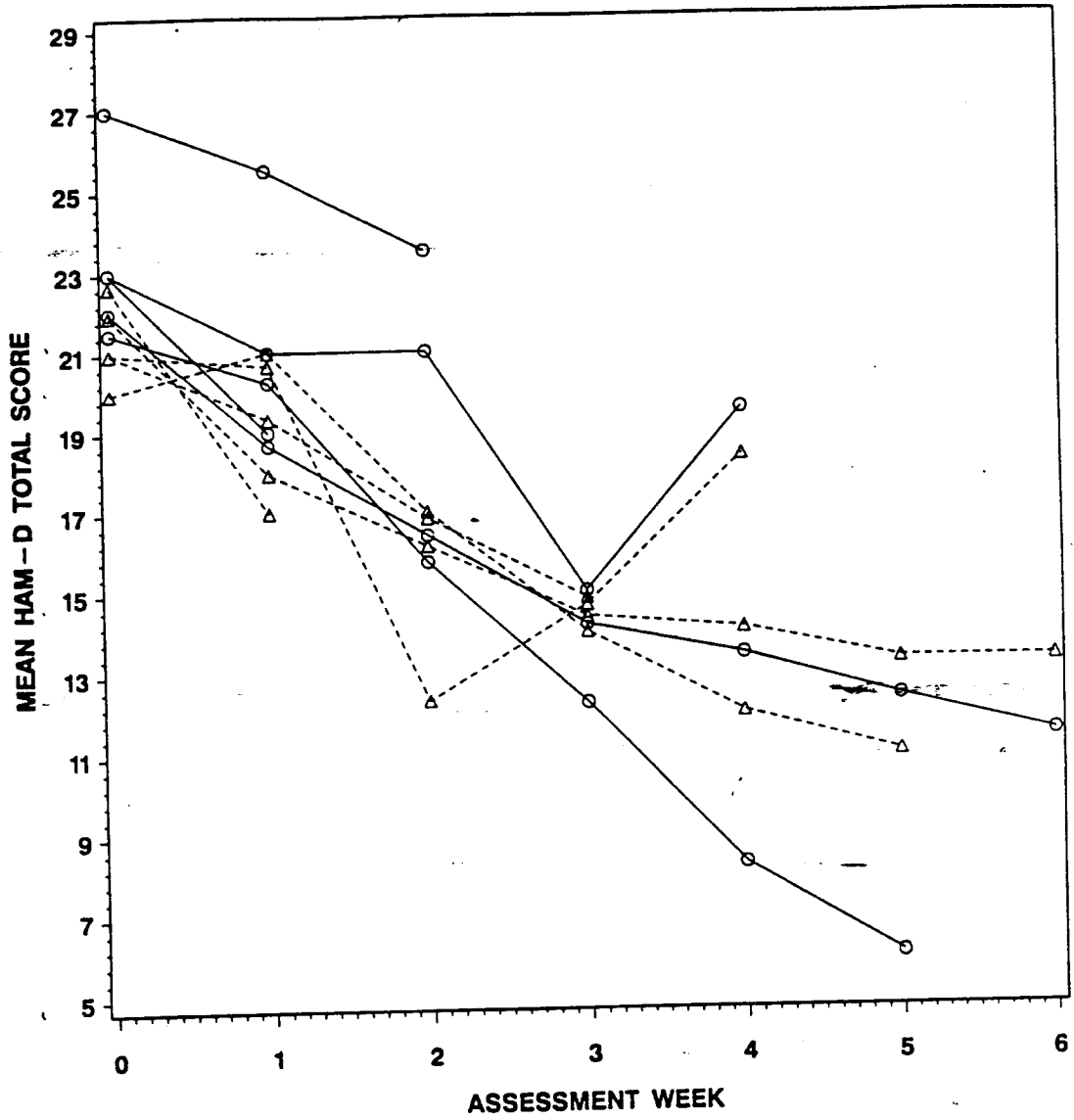
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CITALOPRAM PROTOCOL 91206

2.3.3
FIGURE ~~2-2-3~~
HAM-D TOTAL SCORE



Triangle: Placebo Circle: Citalopram 40 mg

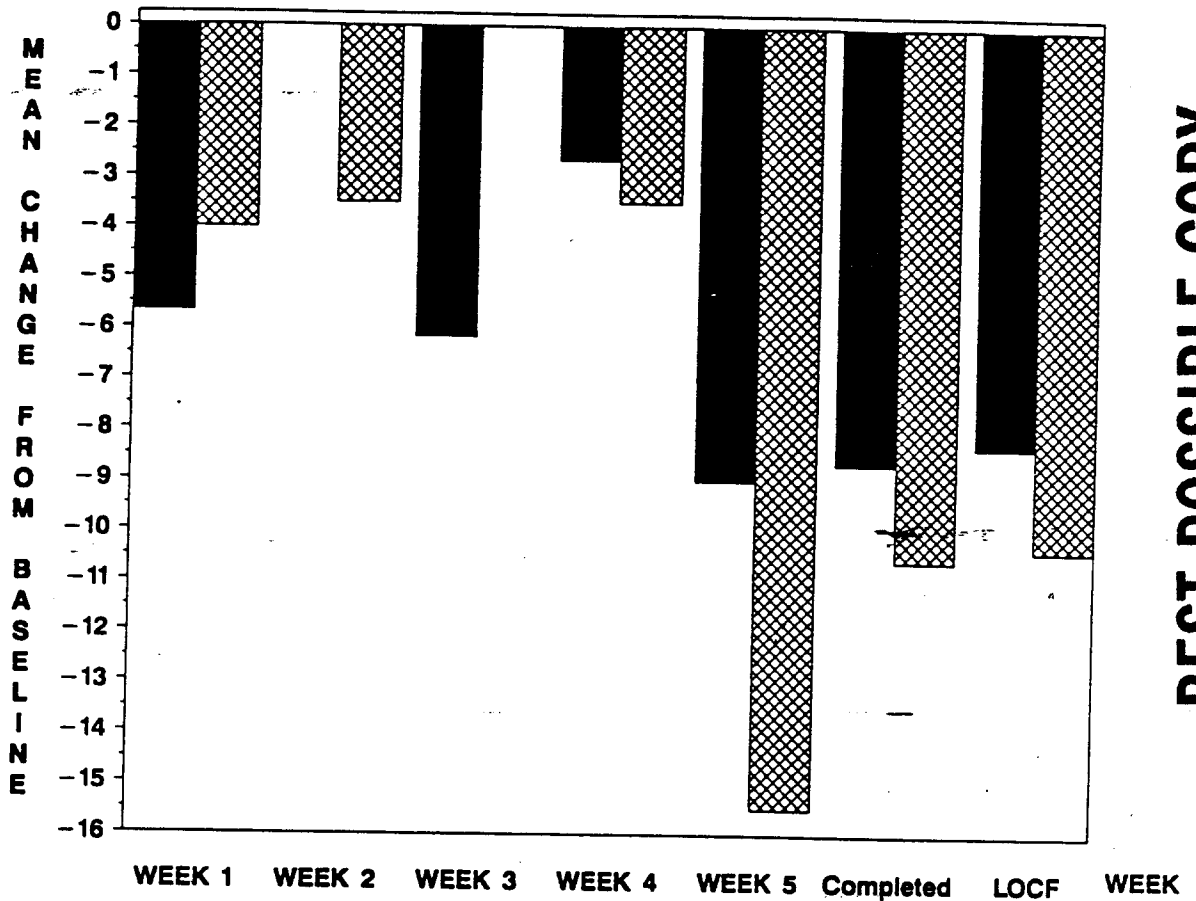
Plot generated by program fig2_206.sas (10FEB97)

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CITALOPRAM PROTOCOL: 91206

2.3.4

FIGURE ~~3-2-3~~
HAMD TOTAL SCORE
AT THE TIME OF DROPOUT, AND COMPLETERS



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■ PLACEBO ▨ 40 mg CIT

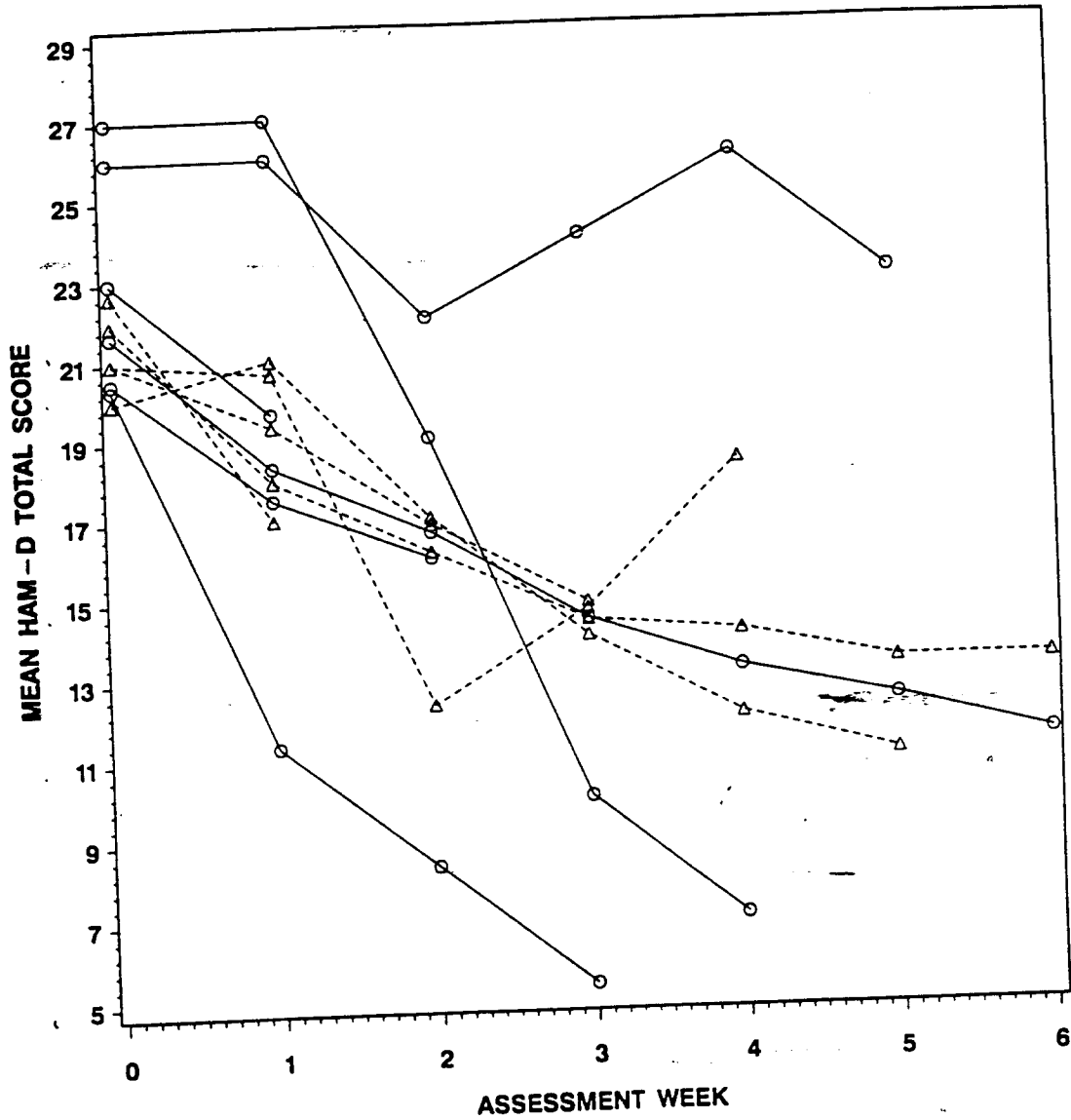
NOTE: Missing bar means no event

Plot generated by program fig3_206.sas (11MAR97)

CITALOPRAM PROTOCOL 91206

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FIGURE ~~2-24~~
HAM-D TOTAL SCORE



Triangle: Placebo Circle: Citalopram 60 mg

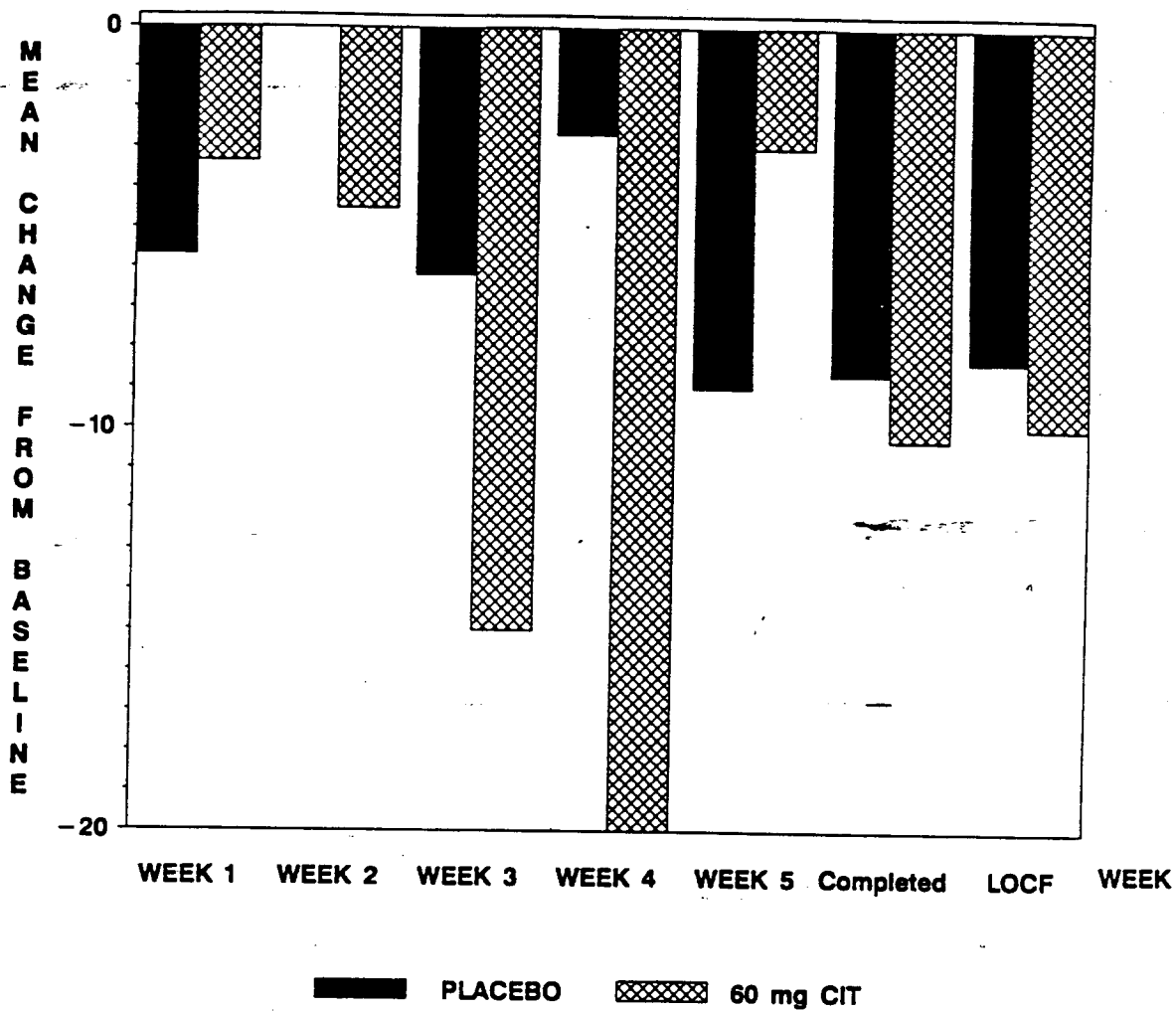
Plot generated by program fig2_206.sas (10FEB97)

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CITALOPRAM PROTOCOL: 91206

2.3.6

FIGURE ~~3-2-4~~
HAMD TOTAL SCORE
AT THE TIME OF DROPOUT, AND COMPLETERS



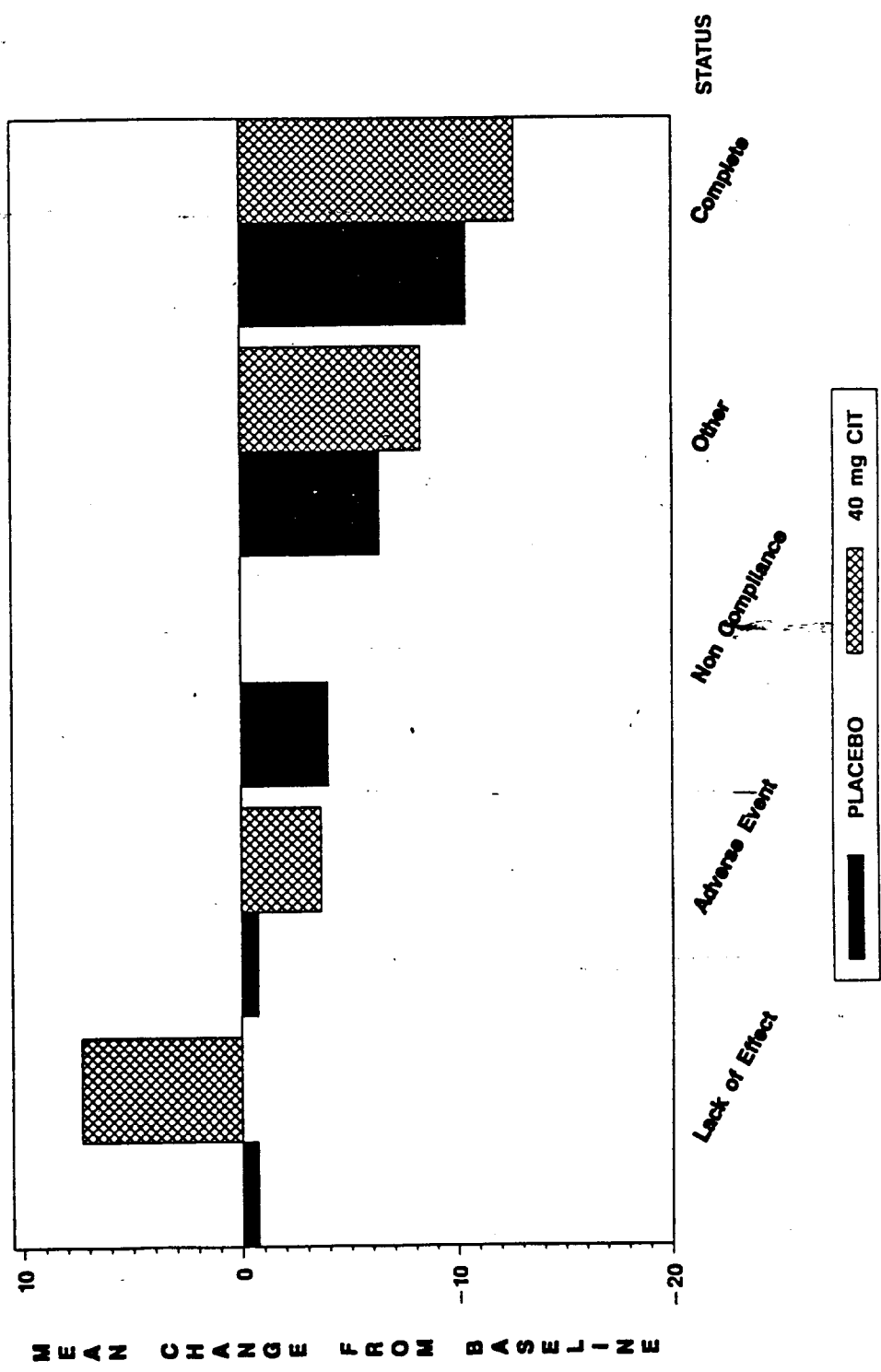
NOTE: Missing bar means no event

Plot generated by program fig3_206.sas (11MAR97)

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CITA RAM PROTOCOL: 91206

FIGURE 4-2-3-2.3.7
HAMD TOTAL SCORE
BY WITHDRAWAL REASON, TOGETHER WITH COMPLETERS



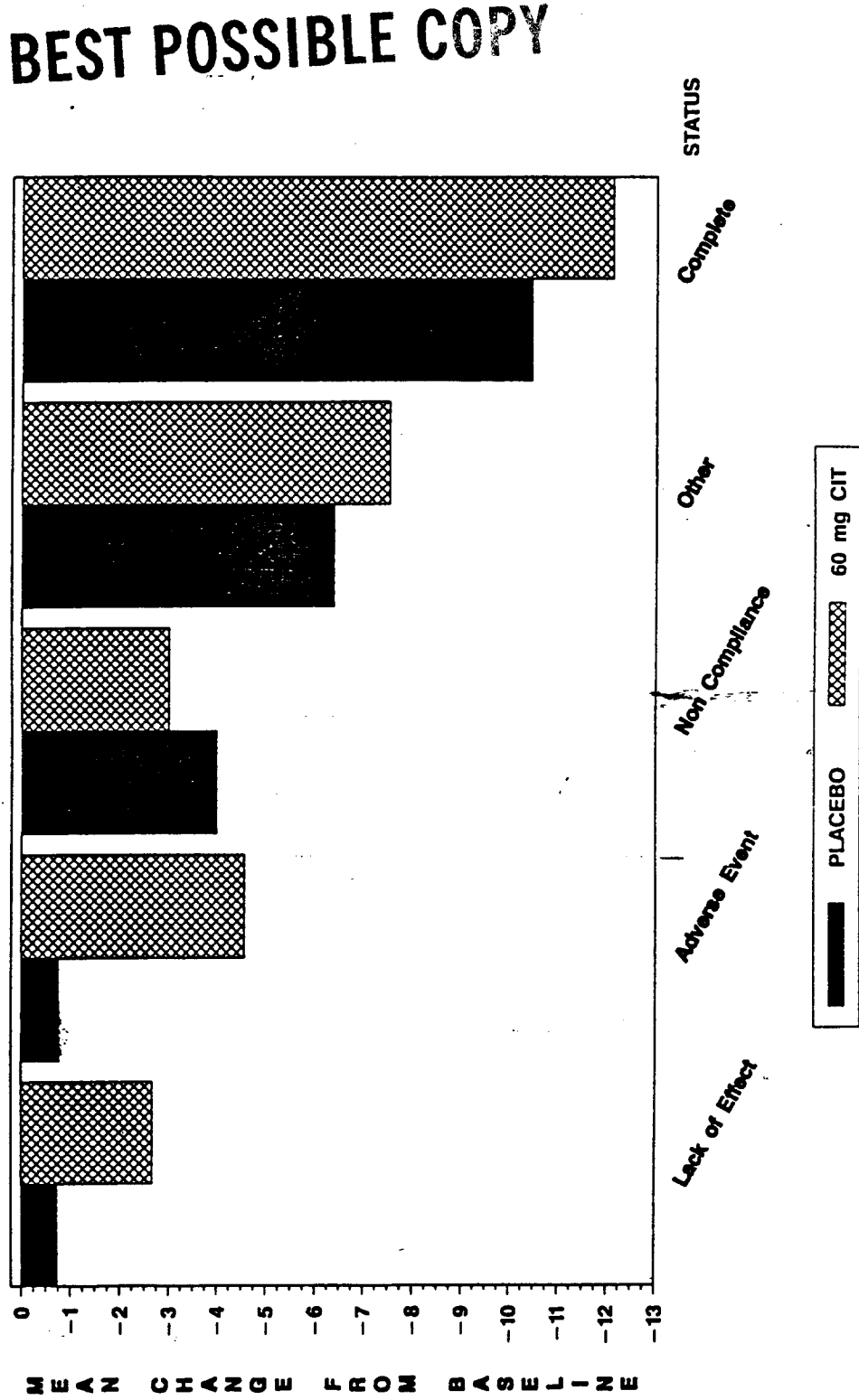
Plot generated by program fig4_206.sas (10FEB97)

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CITAPRAM PROTOCOL: 91206

FIGURE 4-2-4-2.3.8
HAMMD TOTAL SCORE
BY WITHDRAWAL REASON, TOGETHER WITH COMPLETERS



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Table 0703-1-10 2.4.1
 Study: 91206
 Least Square Mean Change from Baseline in HAM-D Depressed Mood Item

LAST OBSERVATION CARRIED FORWARD ANALYSIS

Treatment Groups	Treatment Week																	
	Baseline LS Mean		Week1		Week2		Week3		Week4		Week5		Week6					
	n	x	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ				
CIT 10mg	123	2.93	123	-0.59	123	-0.99	123	-1.18	123	-1.31	123	-1.39	123	-1.46				
CIT 20mg	128	2.86	128	-0.59	128	-0.97	128	-1.18	128	-1.27	128	-1.32	128	-1.38				
CIT 40mg	120	2.86	120	-0.67	120	-0.96	120	-1.28	120	-1.40	120	-1.57	120	-1.61				
CIT 60mg	110	2.88	110	-0.64	110	-1.04	110	-1.31	110	-1.54	110	-1.56	110	-1.71				
PLACEBO	124	2.85	124	-0.43	124	-0.72	124	-0.95	124	-1.06	124	-1.04	124	-1.03				

2-sided p-values for pairwise comparisons from contrast

10mg vs PLAC	0.2205	0.1059	0.0239	0.0622	0.0660	0.0135	0.0031
20mg vs PLAC	0.8987	0.0938	0.0345	0.0589	0.1029	0.0481	0.0155
40mg vs PLAC	0.9940	0.0153	0.0417	0.0077	0.0116	0.0010	0.0010
60mg vs PLAC	0.7346	0.0431	0.0091	0.0045	0.0010	0.0010	0.0010

OBSERVED CASES ANALYSIS

Treatment Groups	Treatment Week																	
	Baseline LS Mean		Week1		Week2		Week3		Week4		Week5		Week6					
	n	x	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ				
CIT 10mg	123	2.93	121	-0.60	116	-1.05	109	-1.24	102	-1.48	94	-1.72	95	-1.81				
CIT 20mg	128	2.86	126	-0.60	114	-0.96	106	-1.21	103	-1.29	92	-1.49	91	-1.55				
CIT 40mg	120	2.86	114	-0.70	106	-1.03	106	-1.41	101	-1.57	93	-1.81	92	-1.84				
CIT 60mg	110	2.88	108	-0.64	103	-1.06	92	-1.39	86	-1.65	79	-1.72	79	-1.93				
PLACEBO	124	2.85	121	-0.44	115	-0.77	112	-1.02	102	-1.20	96	-1.31	88	-1.35				

2-sided p-values for pairwise comparisons from contrast

10mg vs PLAC	0.2205	0.1169	0.0175	0.0775	0.0467	0.0062	0.0025
20mg vs PLAC	0.8987	0.1172	0.1022	0.1471	0.5132	0.2244	0.2024
40mg vs PLAC	0.9940	0.149	0.0297	0.0023	0.0108	0.0010	0.0017
60mg vs PLAC	0.7346	0.0559	0.0171	0.0049	0.0029	0.0090	0.0010

Table 07/03-1-12 2.5

		Study: 91206													
		Least Square Mean Change from Baseline in CGI-severity Score													
		LAST OBSERVATION CARRIED FORWARD ANALYSIS													
Treatment Groups	Baseline LS Mean	Treatment Week													
		Week1		Week2		Week3		Week4		Week5		Week6			
		n	x	n	x	n	x	n	x	n	x	n	x		
CIT 10mg	123	3.28	-0.29	123	-0.59	123	-0.67	123	-0.77	123	-0.82	123	-0.82	123	-0.90
CIT 20mg	128	3.21	-0.26	128	-0.52	128	-0.73	128	-0.73	128	-0.83	128	-0.83	128	-0.81
CIT 40mg	120	3.30	-0.28	120	-0.55	120	-0.75	120	-0.91	120	-0.99	120	-0.99	120	-1.05
CIT 60mg	110	3.21	-0.31	110	-0.47	110	-0.72	110	-0.85	110	-0.90	110	-0.90	110	-1.00
PLACEBO	124	3.27	-0.32	124	-0.52	124	-0.70	124	-0.75	124	-0.80	124	-0.80	124	-0.84
2-sided p-values for pairwise comparisons from contrast															
10mg vs PLAC	0.8260	0.6937		0.3418		0.7579		0.8167		0.8391		0.6089			
20mg vs PLAC	0.1830	0.3635		0.9799		0.6989		0.8624		0.7596		0.7428			
40mg vs PLAC	0.5869	0.5568		0.6740		0.5612		0.0638		0.0557		0.0490			
60mg vs PLAC	0.2150	0.9047		0.4987		0.7483		0.2534		0.3471		0.1317			
OBSERVED CASES ANALYSIS															
Treatment Groups	Baseline LS Mean	Treatment Week													
		Week1		Week2		Week3		Week4		Week5		Week6			
		n	x	n	x	n	x	n	x	n	x	n	x		
CIT 10mg	123	3.28	-0.30	116	-0.64	109	-0.73	102	-0.90	94	-1.06	95	-1.17		
CIT 20mg	128	3.21	-0.26	114	-0.53	106	-0.78	103	-0.78	92	-0.96	91	-0.91		
CIT 40mg	120	3.30	-0.30	106	-0.58	106	-0.80	101	-1.00	93	-1.15	92	-1.19		
CIT 60mg	110	3.21	-0.31	103	-0.47	92	-0.78	86	-0.90	79	-0.97	79	-1.13		
PLACEBO	124	3.27	-0.33	115	-0.54	112	-0.74	102	-0.83	96	-0.98	88	-1.07		
2-sided p-values for pairwise comparisons from contrast															
10mg vs PLAC	0.8260	0.6336		0.1941		0.9418		0.4557		0.4237		0.3755			
20mg vs PLAC	0.1830	0.3227		0.9351		0.6404		0.6298		0.8559		0.1672			
40mg vs PLAC	0.5896	0.6606		0.6182		0.4869		0.0672		0.1118		0.2896			
60mg vs PLAC	0.2150	0.8279		0.4078		0.6557		0.4781		0.9710		0.6093			

Table 07/03-1-11
 Study: 91206
 Least Square Mean Change from Baseline in MADRS Total Score

LAST OBSERVATION CARRIED FORWARD ANALYSIS

Treatment Groups	Treatment Week																							
	Baseline LS Mean		Week1		Week2		Week3		Week4		Week5		Week6											
	n	x	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ										
CIT 10mg	123	27.41	123	-4.33	123	-7.26	123	-8.85	123	-10.56	123	-11.20	123	-11.79										
CIT 20mg	127	26.78	127	-3.84	127	-5.72	127	-8.41	127	-9.74	127	-10.54	127	-11.02										
CIT 40mg	120	27.52	120	-4.34	120	-7.00	120	-9.95	120	-11.35	120	-13.09	120	-13.53										
CIT 60mg	110	27.21	110	-4.36	110	-7.20	110	-10.05	110	-11.66	110	-12.59	110	-13.74										
PLACEBO	124	26.94	124	-3.86	124	-6.38	124	-8.23	124	-9.10	124	-9.39	124	-9.36										

2-sided p-values for pairwise comparisons from contrast

10mg vs PLAC	0.4643	0.5288	0.3349	0.5505	0.1919	0.1304	0.0525
20mg vs PLAC	0.8002	0.9778	0.4633	0.8600	0.5637	0.3302	0.1798
40mg vs PLAC	0.3709	0.5194	0.5015	0.1006	0.0452	0.0022	0.0010
60mg vs PLAC	0.6825	0.5151	0.3832	0.0891	0.0260	0.0097	0.0010

OBSERVED CASES ANALYSIS

Treatment Groups	Treatment Week																							
	Baseline LS Mean		Week1		Week2		Week3		Week4		Week5		Week6											
	n	x	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ	n	Δ										
CIT 10mg	123	27.41	121	-4.38	116	-7.85	109	-9.77	102	-12.47	94	-14.23	95	-15.05										
CIT 20mg	127	26.78	125	-3.87	113	-5.75	105	-8.72	101	-10.31	91	-12.06	90	-12.55										
CIT 40mg	120	27.52	114	-4.57	106	-7.54	106	-10.77	101	-12.57	93	-15.13	92	-15.44										
CIT 60mg	110	27.21	108	-4.39	103	-7.41	92	-10.91	85	-12.64	79	-13.75	79	-15.42										
PLACEBO	124	26.94	121	-3.94	115	-6.80	112	-8.82	102	-10.10	96	-11.48	88	-12.41										

2-sided p-values for pairwise comparisons from contrast

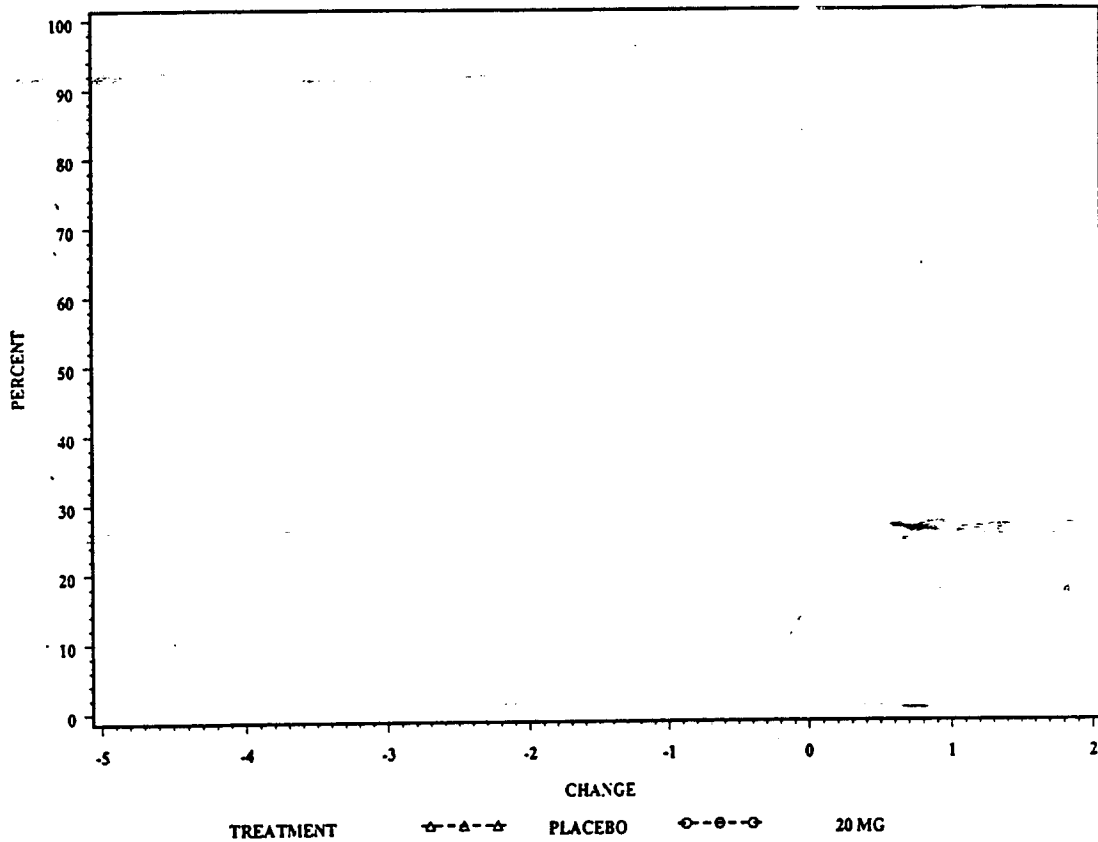
10mg vs PLAC	0.4643	0.5546	0.2483	0.3734	0.0416	0.0252	0.0478
20mg vs PLAC	0.8002	0.9278	0.2551	0.9268	0.8557	0.6428	0.9198
40mg vs PLAC	0.3709	0.4094	0.4323	0.0701	0.0352	0.0032	0.0250
60mg vs PLAC	0.6825	0.5597	0.5180	0.0616	0.0382	0.0772	0.0319

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CITALOPRAM PROTOCOL: 91206

FIGURE (1-3-2) 2.5.29

CHANGE IN CGI-S BASELINE TO LOCF



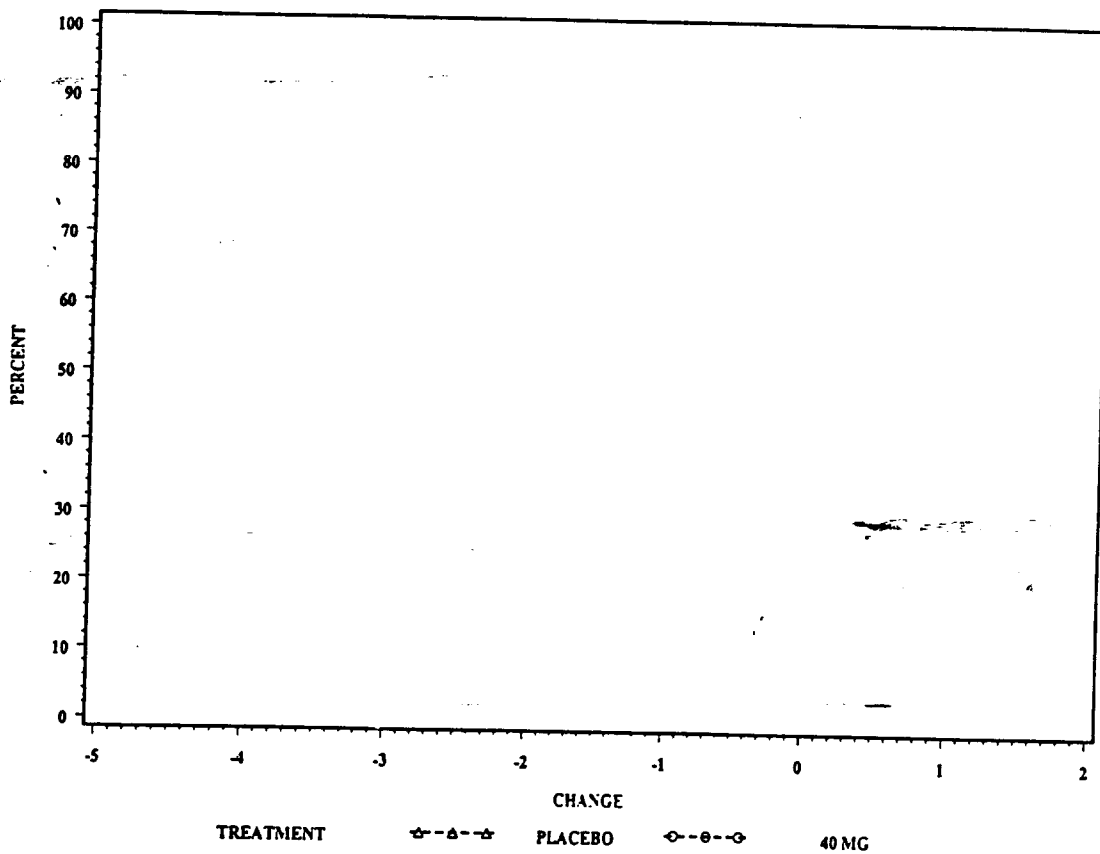
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CITALOPRAM PROTOCOL: 91206

FIGURE (1-3-3) 2.5.25

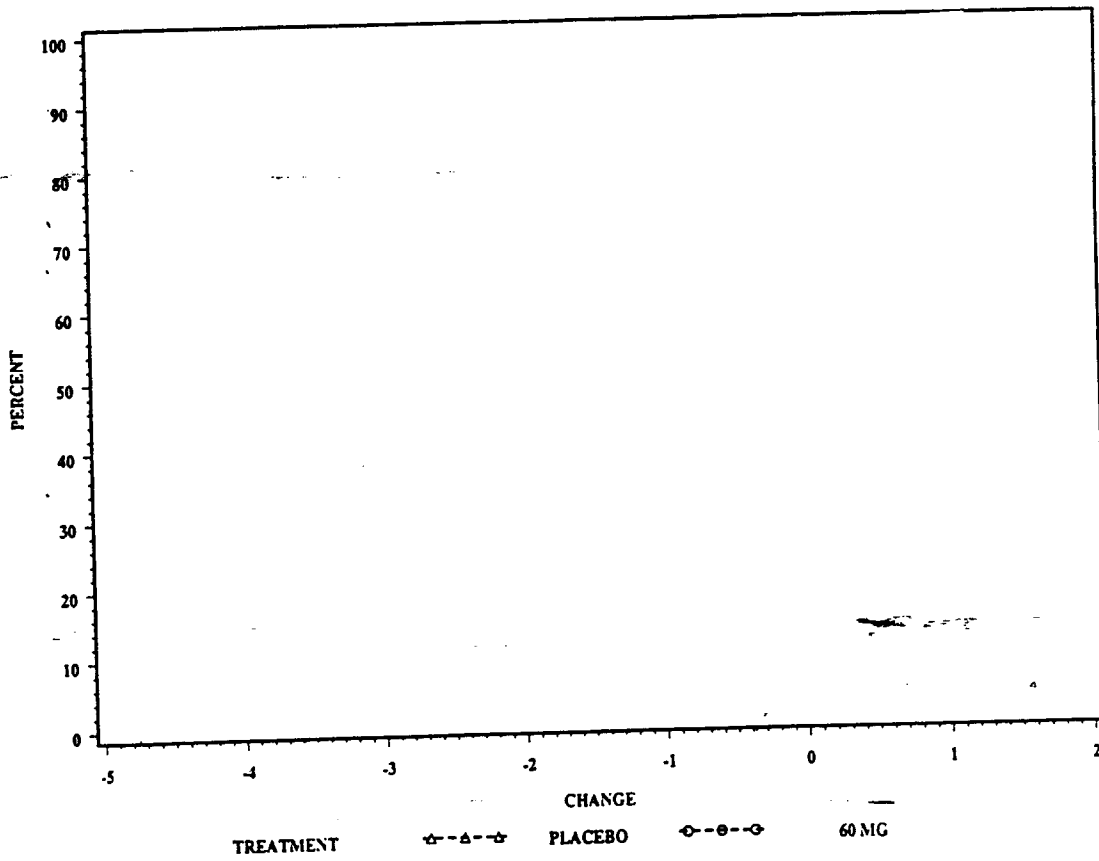
CHANGE IN CGI-S BASELINE TO LOCF



Plot generated by program fig1_206.sas (10FEB97)

CITALOPRAM PROTOCOL: 91206

FIGURE (1-3-4) 2.5.2C
CHANGE IN CGI-S BASELINE TO LOCF



Plot generated by program fig1_206.sas (10FEB97)

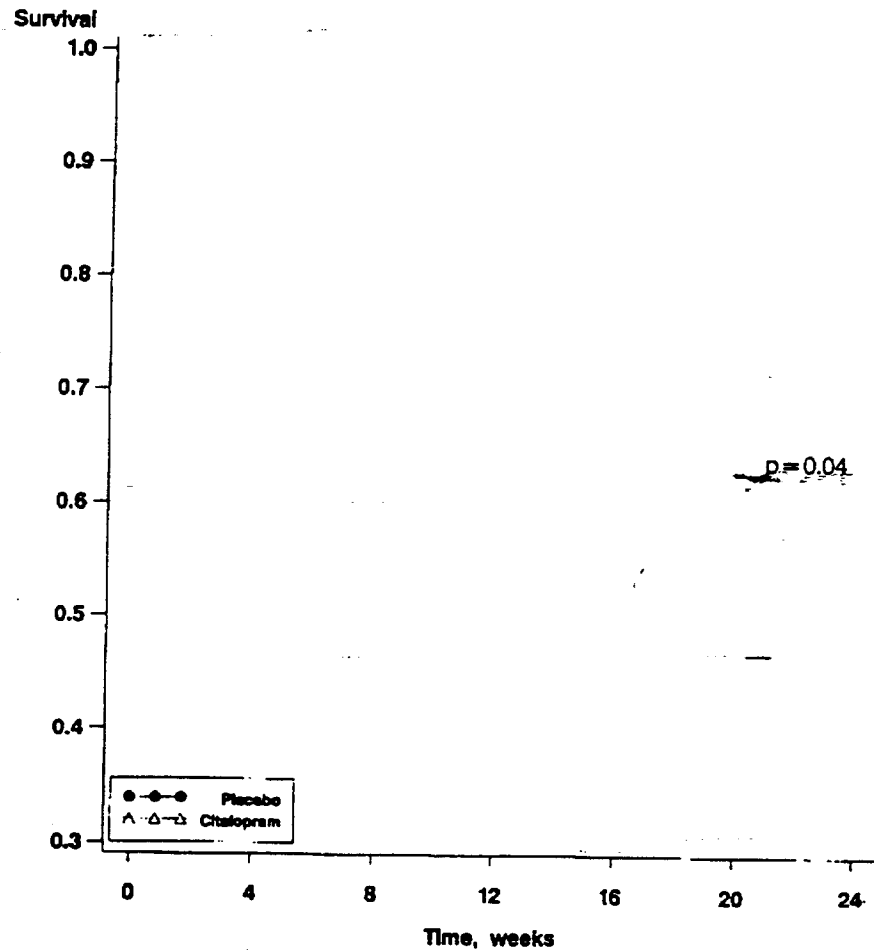
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~~Fig~~ Figure 3.3.1
Panel 4.3.6-3

Survival Curve of Time to Relapse for Study 89304
Placebo-Controlled, Longer-Term
ITT Population



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23 April 1997

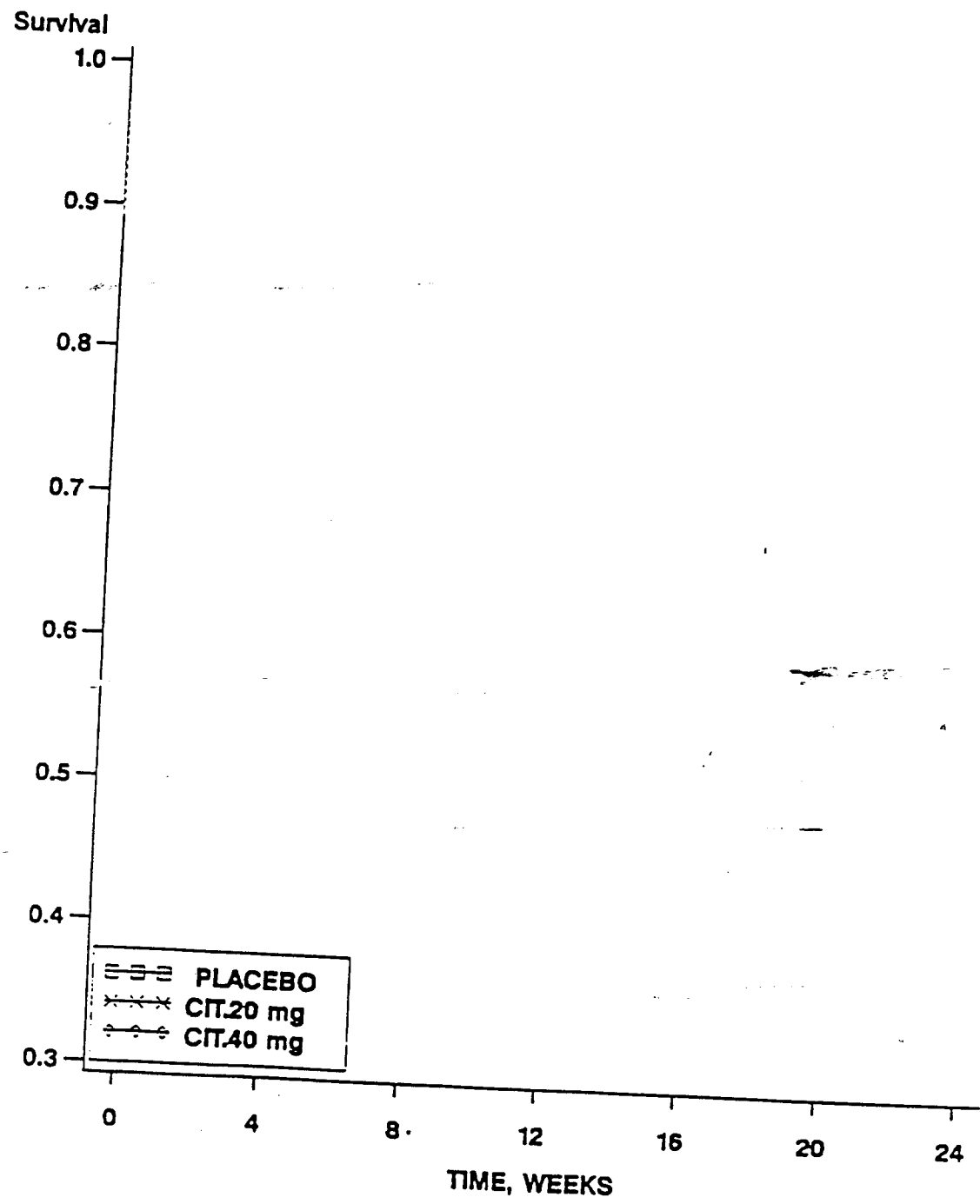
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4.3.1
Figure 4.3 Survival analysis of time until confirmed relapse : Citalopram stratum



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