From: Binder, Carin [JOI]
Sent: Wednesday, May 15, 2002 7:04 PM
To: Pandina, Gahan [JANUS]
Cc: Reyes-Harde, Magali [JANUS]
Subject: FW: RIS-CAN-19/20, USA-93/97, INT-41: Final tables & graphs

Long-term
isperidone vs Prola.

Hi Gahan,

Here are choice selected tables you might like to have slides made for your June 14th meeting. The growth/maturation stuff is still rough and I have a hard copy. Please send me your fax number and I'll fax the 2 main tables to you.

Regards,
Carin

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PLAINTIFF'S EXHIBIT 23

EXHIBIT
Date: P-23
M.L. GRAY, CSR, RPR

Table 3. Patient Demographics and Pre-dose Characteristics: Comparability of PAP vs Non-PAP Populations

Variable	ITT N	ITT Stats	PAP N	PAP Stats	Non-PAP N	Non-PAP Stats	Chi-Square or t-Test p-Value
Gender: N [%]	709		592		117		
Male		580 (81.8)		489 (82.6)		91 (77.8)	0.2165
Female		129 (18.2)		103 (17.4)		26 (22.2)	
Race: N [%]	709		592		117		
Caucasian		557 (78.7)		475 (80.2)		82 (70.7)	0.0234
Black		80 (11.3)		57 (9.6)		23 (19.8)	
Hispanic		12 (1.7)		11 (1.9)		1 (0.9)	
Oriental		3 (0.4)		3 (0.5)		0 (0.0)	
Other		56 (7.9)		46 (7.8)		10 (8.6)	
NA		1		0		1	
Tanner Stage: N[%]	709		592		117		
0		6 (0.9)		4 (0.7)		2 (1.9)	0.3398
1		490 (72.3)		420 (73.0)		70 (68.0)	
2		98 (14.5)		83 (14.4)		15 (14.6)	
3		46 (6.8)		36 (6.3)		10 (9.7)	
4		29 (4.3)		23 (4.0)		6 (5.8)	
5		9 (1.3)		9 (1.6)		0 (0.0)	
NA		31		17		14	
DSM-IV Axis II: N[%]	709		592		117		
Borderline Mental Retardation		291 (41.1)		236 (39.9)		55 (47.0)	0.1596
Mild Mental Retardation		286 (40.4)		248 (42.0)		38 (32.5)	
Moderate Mental Retardation		131 (18.5)		107 (18.1)		24 (20.5)	
NA		1		1		0	
Age [years]	709		592		117		
Mean		9.9		9.9		9.7	0.5203
SD		2.4		2.5		2.3	
Median		9.9		9.9		9.9	
Minimum		5.0		5.1		5.0	
Maximum		15.0		15.0		14.7	
IQ Rating	708		591		117		
Mean		65.1		65.1		65.1	0.9644
SD		13.4		13.3		14.0	
Median		68.0		68.0		68.0	
Minimum		35.0		36.0		35.0	
Maximum		84.0		84.0		84.0	
Height [cm]	688		573		115		
Mean		137.5		137.8		136.2	0.3210
SD		15.6		15.9		14.3	

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Table 3. Patient Demographics and Pre-dose Characteristics: Comparability of PAP vs Non-PAP Populations -(continued)

Variable	ITT N	ITT Stats	PAP N	PAP Stats	Non-PAP N	Non-PAP Stats	Chi-Square or t-Test p-Value
Median		137.0		137.0		136.9	
Minimum		99.1		99.1		101.6	
Maximum		192.0		192.0		172.7	
Weight [kg]	707		591		116		
Mean		35.1		35.4		33.9	0.2719
SD		13.1		13.4		11.6	
Median		32.1		32.1		32.2	
Minimum		13.6		14.0		13.6	
Maximum		87.8		87.8		82.1	
BMI	687		573		114		
Mean		18.0		18.0		17.9	0.8637
SD		3.7		3.7		3.8	
Median		17.1		17.1		17.1	
Minimum		8.8		8.8		12.7	
Maximum		35.3		33.4		35.3	

Table 4. Study Drug Dosing Information: Comparability of PAP vs Non-PAP Populations

Study Drug Dosing Variable	ITT N	ITT Stats	PAP N	PAP Stats	Non-PAP N	Non-PAP Stats	t- Test p-Value
Study Drug Exposure [mg]*	700		592		108		
Mean		396.93		410.05		325.01	0.0081
SD		274.48		265.94		308.79	
Median		393.95		411.00		276.93	
Minimum		0.30		0.40		0.30	
Maximum		1305.80		1305.80		1274.80	
Study Drug Duration [days]**	700		592		108		
Mean		307.87		319.40		244.66	<0.0001
SD		116.14		101.26		163.42	
Median		359.00		361.00		336.00	
Minimum		1.00		28.00		1.00	
Maximum		505.00		505.00		498.00	
Average Daily Dose [mg]***	700		592		108		
Mean		1.23		1.26		1.05	0.0051
SD		0.72		0.70		0.77	
Median		1.20		1.22		0.96	
Minimum		0.00		0.00		0.02	
Maximum		4.17		4.17		3.48	

*Study drug exposure = Area under the Dose x Time curve
**Study drug duration = Date of last dose - Date of first dose + 1
***Average daily dose = Exposure / Study drug duration

Note. No dose was recorded for the following two patient (PAP):
-patient A03306 from 28MAY1998 to 16JUN1998
-patient A03974 from 17JAN2000 to 20JAN2000

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Table 6. Prolactin Levels in Each Period (PAP - As Observed): Descriptive Statistics

Time Period	N	Mean	SD	Median	Minimum	Maximum
Pre-dose	592	7.8	7.2	5.7	2.0	76.5
Weeks 4 to 7	550	29.4	16.5	26.9	2.0	150.0
Weeks 8 to 12	499	23.4	17.0	20.5	1.0	153.0
Weeks 16 to 24	441	19.6	14.5	16.7	2.0	90.9
Weeks 28 to 36	394	18.5	13.5	15.9	2.0	102.0
Weeks 40 to 48	358	16.1	13.2	13.7	1.9	160.9
Weeks 52 to 55	42	13.0	14.1	10.0	2.0	88.0

Table 7. Incidence of Prolactin Levels at or above Upper Limit of Normal (ULN) in Each Period (PAP - As Observed): Number [%] of Patients

Time Period	N	Incidence of Prolactin	
		Above ULN*	Normal
Pre-dose	592	29 (4.9)	563 (95.1)
Weeks 4 to 7	550	388 (70.5)	162 (29.5)
Weeks 8 to 12	499	257 (51.5)	242 (48.5)
Weeks 16 to 24	441	176 (39.9)	265 (60.1)
Weeks 28 to 36	394	148 (37.6)	246 (62.4)
Weeks 40 to 48	358	110 (30.7)	248 (69.3)
Weeks 52 to 55	42	7 (16.7)	35 (83.3)

*ULN: The upper limit of normal for prolactin levels is 18 for males and 30 for females

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Table 8. Prolactin Levels in Each Period (PAP - Fixed N Subsets): Descriptive Statistics

Fixed N Subset*	Time Period	N	Mean	SD	Median	Minimum	Maximum
Pre-dose and Weeks 4 to 7	Pre-dose	550	7.7	7.2	5.7	2.0	76.5
	Weeks 4 to 7	550	29.4	16.5	26.9	2.0	150.0
Pre-dose, Weeks 4 to 7 and 8 to 12	Pre-dose	466	7.7	7.5	5.7	2.0	76.5
	Weeks 4 to 7	466	29.5	16.3	27.0	2.0	150.0
	Weeks 8 to 12	466	23.5	17.0	20.8	1.0	153.0
Pre-dose, Weeks 4 to 7, 8 to 12 and 16 to 24	Pre-dose	385	7.6	7.0	5.5	2.0	50.7
	Weeks 4 to 7	385	30.1	16.5	27.6	2.9	150.0
	Weeks 8 to 12	385	24.5	17.8	21.3	1.0	153.0
	Weeks 16 to 24	385	19.8	14.9	16.7	2.0	90.9
Pre-dose, Weeks 4 to 7, 8 to 12, 16 to 24 and 28 to 36	Pre-dose	318	7.5	6.7	5.4	2.0	47.7
	Weeks 4 to 7	318	30.1	16.4	27.4	2.9	150.0
	Weeks 8 to 12	318	24.3	16.6	22.0	1.0	103.0
	Weeks 16 to 24	318	19.7	14.4	16.9	2.0	90.9
	Weeks 28 to 36	318	18.4	13.0	15.9	2.0	102.0
Pre-dose, Weeks 4 to 7, 8 to 12, 16 to 24, 28 to 36 and 40 to 48	Pre-dose	269	7.4	6.6	5.2	2.0	47.0
	Weeks 4 to 7	269	29.7	14.9	27.0	2.9	83.6
	Weeks 8 to 12	269	24.3	16.1	22.0	1.0	103.0
	Weeks 16 to 24	269	19.6	14.0	16.7	2.0	88.0
	Weeks 28 to 36	269	18.4	12.8	15.7	2.0	102.0
	Weeks 40 to 48	269	15.6	11.0	13.6	1.9	61.6
Pre-dose, Weeks 4 to 7, 8 to 12, 16 to 24, 28 to 36, 40 to 48 and 52 to 55	Pre-dose	22	7.7	7.5	7.0	2.0	39.0
	Weeks 4 to 7	22	27.8	19.3	24.5	4.0	82.0
	Weeks 8 to 12	22	26.5	26.7	18.3	3.8	103.0
	Weeks 16 to 24	22	15.4	16.7	10.2	3.0	83.0
	Weeks 28 to 36	22	17.5	20.6	12.7	2.0	102.0
	Weeks 40 to 48	22	17.7	11.9	15.0	2.0	51.0
	Weeks 52 to 55	22	14.3	17.9	10.2	2.0	88.0

*To be included in a subset, observations had to exist at every time period in that subset

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Table 11. Prolactin Levels [ng/mL] by Gender and Time Period (PAP - As Observed): Descriptive Statistics

	Prolactin											
	Males						Females					
Time Period	N	Mean	SD	Median	Minimum	Maximum	N	Mean	SD	Median	Minimum	Maximum
Pre-dose	489	7.3	7.0	5.1	2.0	76.5	103	10.0	7.8	7.0	2.0	50.7
Weeks 4 to 7	457	28.8	16.0	26.7	2.0	150.0	93	32.7	18.3	29.3	3.0	95.2
Weeks 8 to 12	417	22.8	17.0	19.3	1.0	153.0	82	26.6	16.5	25.0	2.0	78.0
Weeks 16 to 24	369	18.9	14.0	16.1	2.0	90.9	72	23.5	16.2	19.2	3.3	81.3
Weeks 28 to 36	323	17.6	12.3	15.1	2.0	102.0	71	22.5	17.4	19.0	2.0	79.8
Weeks 40 to 48	303	15.1	10.4	13.0	1.9	61.6	55	21.4	22.7	16.0	2.0	160.9
Weeks 52 to 55	34	13.0	15.1	9.0	2.0	88.0	8	12.9	8.9	10.5	5.0	33.0

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Table 12. Prolactin Levels [ng/mL] by Age Group [years] and Time Period (PAP - As Observed): Descriptive Statistics

		Prolactin					
Age Group	Time Period	N	Mean	SD	Median	Minimum	Maximum
5 to 7	Pre-dose	114	8.0	6.6	6.2	2.0	46.8
	Weeks 4 to 7	106	29.9	17.9	26.0	3.0	101.8
	Weeks 8 to 12	87	21.5	17.3	18.3	1.0	88.0
	Weeks 16 to 24	73	18.4	14.2	15.0	2.9	83.0
	Weeks 28 to 36	76	18.8	15.4	15.5	2.0	102.0
	Weeks 40 to 48	65	14.6	10.3	12.4	2.0	44.0
	Weeks 52 to 55	12	16.9	23.3	10.2	3.0	88.0
8 to 9	Pre-dose	146	7.6	6.3	5.5	2.0	40.2
	Weeks 4 to 7	133	28.5	15.9	27.0	2.9	99.0
	Weeks 8 to 12	122	23.5	14.7	21.1	3.0	82.4
	Weeks 16 to 24	108	18.1	11.5	16.1	2.0	55.0
	Weeks 28 to 36	97	15.5	10.0	13.4	2.0	47.0
	Weeks 40 to 48	95	14.4	10.3	12.0	2.0	44.0
	Weeks 52 to 55	11	9.2	9.0	6.0	2.0	33.0
10 to 11	Pre-dose	162	6.9	6.7	5.0	2.0	47.7
	Weeks 4 to 7	148	29.0	17.0	26.9	2.0	150.0
	Weeks 8 to 12	141	23.0	17.2	18.4	2.0	103.0
	Weeks 16 to 24	123	18.3	14.4	14.0	2.0	90.9
	Weeks 28 to 36	107	18.2	14.3	15.0	2.0	87.7
	Weeks 40 to 48	94	16.2	12.4	13.7	1.9	61.6
	Weeks 52 to 55	13	10.7	6.0	10.0	4.0	25.3
12 to 15	Pre-dose	170	8.6	8.7	6.0	2.0	76.5
	Weeks 4 to 7	163	30.3	15.7	27.6	3.0	95.2
	Weeks 8 to 12	149	24.9	18.2	23.0	2.0	153.0
	Weeks 16 to 24	137	22.7	16.3	19.0	2.5	88.0
	Weeks 28 to 36	114	20.9	13.7	19.3	3.1	79.8
	Weeks 40 to 48	104	18.4	17.2	16.0	2.0	160.9
	Weeks 52 to 55	6	16.9	9.4	13.0	6.0	29.0

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Table 13. Prolactin Levels [ng/mL] by Gender and Age Group [years] (PAP - As Observed): Descriptive Statistics

			Prolactin [ng/mL]					
Time Period	Gender	Age Category	N	Mean	SD	Median	Minimum	Maximum
Pre-dose	Male	>= 10	234	7.3	8.0	5.0	2.0	76.5
		< 10	255	7.3	6.0	5.7	2.0	46.8
		Total	489	7.3	7.0	5.1	2.0	76.5
	Female	>= 9	59	10.3	8.2	7.2	2.0	50.7
		< 9	44	9.7	7.3	7.0	2.5	39.0
		Total	103	10.0	7.8	7.0	2.0	50.7
Weeks 4 to 7	Male	>= 10	222	28.6	15.8	26.3	2.0	150.0
		< 10	235	29.0	16.3	26.9	2.9	101.8
		Total	457	28.8	16.0	26.7	2.0	150.0
	Female	>= 9	54	34.6	19.1	31.1	3.0	95.2
		< 9	39	29.9	17.1	26.0	3.0	70.0
		Total	93	32.7	18.3	29.3	3.0	95.2
Weeks 8 to 12	Male	>= 10	209	22.9	17.4	19.3	2.0	153.0
		< 10	208	22.8	16.6	19.7	1.0	88.0
		Total	417	22.8	17.0	19.3	1.0	153.0
	Female	>= 9	48	30.0	17.4	29.1	2.0	78.0
		< 9	34	21.8	13.9	20.9	3.0	53.0
		Total	82	26.6	16.5	25.0	2.0	78.0
Weeks 16 to 24	Male	>= 10	191	19.5	14.7	16.8	2.0	90.9
		< 10	178	18.2	13.2	15.1	2.0	83.0
		Total	369	18.9	14.0	16.1	2.0	90.9
	Female	>= 9	43	26.9	18.2	21.2	3.3	81.3
		< 9	29	18.5	11.1	15.6	3.9	42.0
		Total	72	23.5	16.2	19.2	3.3	81.3
Weeks 28 to 36	Male	>= 10	156	18.4	11.9	16.9	2.0	87.7
		< 10	167	16.8	12.7	13.8	2.0	102.0
		Total	323	17.6	12.3	15.1	2.0	102.0
	Female	>= 9	46	26.1	19.4	21.0	2.4	79.8
		< 9	25	15.8	10.4	13.9	2.0	41.0
		Total	71	22.5	17.4	19.0	2.0	79.8
Weeks 40 to 48	Male	>= 10	149	14.8	9.1	14.5	1.9	48.5
		< 10	154	15.4	11.6	12.3	2.0	61.6
		Total	303	15.1	10.4	13.0	1.9	61.6

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Table 13. Prolactin Levels [ng/mL] by Gender and Age Group [years] (PAP - As Observed): Descriptive Statistics -(continued)

Time Period	Gender	Age Category	Prolactin [ng/mL] N	Mean	SD	Median	Minimum	Maximum
Weeks 40 to 48	Female	>= 9	31	25.3	27.7	20.2	5.0	160.9
		< 9	24	16.2	12.6	13.3	2.0	44.0
		Total	55	21.4	22.7	16.0	2.0	160.9
Weeks 52 to 55	Male	>= 10	16	13.1	8.0	12.7	4.0	29.0
		< 10	18	12.9	19.7	6.8	2.0	88.0
		Total	34	13.0	15.1	9.0	2.0	88.0
	Female	>= 9	2	8.0	2.8	8.0	6.0	10.0
		< 9	6	14.5	9.8	11.0	5.0	33.0
		Total	8	12.9	8.9	10.5	5.0	33.0

Table 16. Incidence of Prolactin-related Side Effects (PAP vs Non-Pap): Number [%] of Patients

System Organ Class	Preferred Term	ITT	PAP	Non-PAP
Total Number of Patients		709	592	117
Number of Patients with at Least One Prolactin-related Side Effect		34 (4.8)	30 (5.1)	4 (3.4)
ENDOCRINE DISORDERS	GYNAECOMASTIA	25 (3.5)	22 (3.7)	3 (2.6)
REPRODUCTIVE DISORDERS, FEMALE	AMENORRHOEA	4 (0.6)	3 (0.5)	1 (0.9)
	MENORRHAGIA	3 (0.4)	3 (0.5)	0 (0.0)
	BREAST ENLARGEMENT	1 (0.1)	1 (0.2)	0 (0.0)
	LACTATION NONPUERPERAL	1 (0.1)	1 (0.2)	0 (0.0)
	MENSTRUAL DISORDER	1 (0.1)	1 (0.2)	0 (0.0)
	VAGINAL HAEMORRHAGE	1 (0.1)	1 (0.2)	0 (0.0)

Note 1) Prolactin-related side effects are adverse events classified under System Organ Class as "Endocrine disorders" or "Reproductive disorders"

2) Prolactin-related side effects classified under Preferred Term as "Balanoposthitis", "Dysmenorrhoea", "Growth Hormone Excess", "Hernia Inguinal", "Hyperprolactinaemia", "Penis Disorder", "Sexual Function Abnormal", "Sialoadenitis", "Testis Disorder", "Thyroiditis", "Thyroid Stim. Hormone Decreased" and "Vaginitis Atrophic" were not included

3) Multiple occurrences of a side effect within a patient are counted only once

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Table 17. Onset of Prolactin-related Side Effects (PAP - As Observed): Descriptive Statistics

Number of Patients with Prolactin-related Side Effects	Duration [days] from Pre-dose*						
	Mean	SD	25th	50th	75th	Minimum	Maximum
30	142.5	102.2	62	126	177	24	379

*Onset of first prolactin-related side effect

Note 1) Prolactin-related side effects are adverse events classified under System Organ Class as "Endocrine disorders" or "Reproductive disorders"

2) Prolactin-related side effects classified under Preferred Term as "Balanoposthitis", "Dysmenorrhoea", "Growth Hormone Excess", "Hernia Inguinal", "Hyperprolactinaemia", "Penis Disorder", "Sexual Function Abnormal", "Sialoadenitis", "Testis Disorder", "Thyroiditis", "Thyroid Stim. Hormone Decreased" and "Vaginitis Atrophic" were not included

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Table 19. Study Drug Dosing Information by Prolactin-related Side Effects (PAP - As Observed): Descriptive Statistics

	Patients with Side Effects (at any time)						Patients without Side Effects					
Study Drug Dosing Variable	N	Mean	SD	Median	Minimum	Maximum	N	Mean	SD	Median	Minimum	Maximum
Study Drug Exposure [mg]*	30	439.83	279.17	436.95	40.22	1048.77	562	408.46	265.38	406.60	0.40	1305.80
Study Drug Duration [days]**	30	336.57	74.60	364.50	84.00	414.00	562	318.48	102.46	360.00	28.00	505.00
Average Daily Dose [mg]***	30	1.27	0.72	1.20	0.12	2.80	562	1.26	0.70	1.23	0.00	4.17

*Study drug exposure = Area under the Dose x Time curve
**Study drug duration = Date of last dose - Date of first dose + 1
***Average daily dose = Exposure / Study drug duration
Note 1) Prolactin-related side effects are adverse events classified under System Organ Class as "Endocrine disorders" or "Reproductive disorders"
2) Prolactin-related side effects classified under Preferred Term as "Balanoposthitis", "Dysmenorrhoea", "Growth Hormone Excess", "Hernia Inguinal", "Hyperprolactinaemia", "Penis Disorder", "Sexual Function Abnormal", "Sialoadenitis", "Testis Disorder", "Thyroiditis", "Thyroid Stim. Hormone Decreased" and "Vaginitis Atrophic" were not included
3) No dose was recorded for the following two patient:
-patient A03306 from 28MAY1998 to 16JUN1998
-patient A03974 from 17JAN2000 to 20JAN2000

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Table 21. Prolactin-related Side Effects by Prolactin Levels [ng/mL] at or above Upper Limit of Normal (ULN) (PAP - As Observed): Frequency Tables

Time Period	Prolactin-related Side Effects	N	Prolactin		Chi-Square Test p-Value
			Above ULN*	Normal	
Pre-dose	Yes		2 (6.9)	28 (5.0)	0.6452
	No		27 (93.1)	535 (95.0)	
	Total	592	29	563	
Weeks 4 to 7	Yes		21 (5.4)	6 (3.7)	0.3979
	No		367 (94.6)	156 (96.3)	
	Total	550	388	162	
Weeks 8 to 12	Yes		20 (7.8)	7 (2.9)	0.0158
	No		237 (92.2)	235 (97.1)	
	Total	499	257	242	
Weeks 16 to 24	Yes		9 (5.1)	17 (6.4)	0.5699
	No		167 (94.9)	248 (93.6)	
	Total	441	176	265	
Weeks 28 to 36	Yes		7 (4.7)	16 (6.5)	0.4669
	No		141 (95.3)	230 (93.5)	
	Total	394	148	246	
Weeks 40 to 48	Yes		6 (5.5)	14 (5.6)	0.9422
	No		104 (94.5)	234 (94.4)	
	Total	358	110	248	

*ULN: The upper limit of normal for prolactin levels is 18 for males and 30 for females

Note 1) Prolactin-related side effects are adverse events classified under System Organ Class as "Endocrine disorders" or "Reproductive disorders"

2) Prolactin-related side effects classified under Preferred Term as "Balanoposthitis", "Dysmenorrhoea", "Growth Hormone Excess", "Hernia Inguinal", "Hyperprolactinaemia", "Penis Disorder", "Sexual Function Abnormal", "Sialoadenitis", "Testis Disorder", "Thyroiditis", "Thyroid Stim. Hormone Decreased" and "Vaginitis Atrophic" were not included

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Table 28. Prolactin Levels [ng/mL] by Extrapyramidal Symptoms (EPS) (PAP - As Observed): Descriptive Statistics

Time Period	Patients with EPS (at any time)						Patients without EPS					
	N	Mean	SD	Median	Minimum	Maximum	N	Mean	SD	Median	Minimum	Maximum
Pre-dose	140	8.7	8.8	5.7	2.0	47.7	452	7.5	6.7	5.7	2.0	76.5
Weeks 4 to 7	128	30.6	19.2	25.9	3.0	150.0	422	29.1	15.6	27.0	2.0	101.8
Weeks 8 to 12	124	26.4	19.5	20.8	3.0	103.0	375	22.5	15.9	20.0	1.0	153.0
Weeks 16 to 24	114	19.2	16.4	14.5	2.0	90.9	327	19.7	13.7	17.0	2.0	83.4
Weeks 28 to 36	102	19.4	16.1	13.9	2.0	87.7	292	18.1	12.5	16.0	2.0	102.0
Weeks 40 to 48	88	17.5	18.6	13.1	2.0	160.9	270	15.6	11.0	13.7	1.9	61.6
Weeks 52 to 55	13	6.7	4.3	5.0	2.0	16.0	29	15.8	16.0	11.0	2.0	88.0

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Table 30. Extrapyramidal Symptoms (EPS) by Prolactin Levels at or above Upper Limit of Normal (ULN) (PAP - As Observed): Frequency Tables

Time Period	EPS	N	Prolactin [ng/mL] Above ULN*	Prolactin [ng/mL] Normal	Chi-Square Test/p-Value
Pre-dose	Yes		8 (27.6)	132 (23.4)	0.6089
	No		21 (72.4)	431 (76.6)	
	Total	592	29	563	
Weeks 4 to 7	Yes		91 (23.5)	37 (22.8)	0.8765
	No		297 (76.5)	125 (77.2)	
	Total	550	388	162	
Weeks 8 to 12	Yes		65 (25.3)	59 (24.4)	0.8138
	No		192 (74.7)	183 (75.6)	
	Total	499	257	242	
Weeks 16 to 24	Yes		40 (22.7)	74 (27.9)	0.2222
	No		136 (77.3)	191 (72.1)	
	Total	441	176	265	
Weeks 28 to 36	Yes		39 (26.4)	63 (25.6)	0.8707
	No		109 (73.6)	183 (74.4)	
	Total	394	148	246	
Weeks 40 to 48	Yes		25 (22.7)	63 (25.4)	0.5875
	No		85 (77.3)	185 (74.6)	
	Total	358	110	248	

*ULN: The upper limit of normal for prolactin levels is 18 for males and 30 for females

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Table 34. Responders on the Conduct Problem Subscale of the N-CBRF by Prolactin Levels [ng/mL] (PAP - As Observed): Frequency Tables

Response Criteria	Time Period	Responders	N	Above ULN*	Normal	Chi-Square Test p-Value
>= 25% vs < 25%	Weeks 4 to 7	Yes		195 (80.2)	76 (82.6)	0.6236
		No		48 (19.8)	16 (17.4)	
		Total	335	243	92	
	Weeks 8 to 12	Yes		149 (81.4)	117 (79.6)	0.6762
		No		34 (18.6)	30 (20.4)	
		Total	330	183	147	
	Weeks 16 to 24	Yes		107 (84.9)	145 (75.1)	0.0358
		No		19 (15.1)	48 (24.9)	
		Total	319	126	193	
	Weeks 28 to 36	Yes		101 (83.5)	150 (76.9)	0.1616
		No		20 (16.5)	45 (23.1)	
		Total	316	121	195	
	Weeks 40 to 48	Yes		86 (78.9)	202 (82.4)	0.4286
		No		23 (21.1)	43 (17.6)	
		Total	354	109	245	
>= 35% vs < 35%	Weeks 4 to 7	Yes		173 (71.2)	67 (72.8)	0.7673
		No		70 (28.8)	25 (27.2)	
		Total	335	243	92	
	Weeks 8 to 12	Yes		132 (72.1)	104 (70.7)	0.7821
		No		51 (27.9)	43 (29.3)	
		Total	330	183	147	
	Weeks 16 to 24	Yes		97 (77.0)	128 (66.3)	0.0411
		No		29 (23.0)	65 (33.7)	
		Total	319	126	193	
	Weeks 28 to 36	Yes		88 (72.7)	138 (70.8)	0.7077
		No		33 (27.3)	57 (29.2)	
		Total	316	121	195	
	Weeks 40 to 48	Yes		76 (69.7)	181 (73.9)	0.4187
		No		33 (30.3)	64 (26.1)	
		Total	354	109	245	

*ULN: The upper limit of normal for prolactin levels is 18 for boys and 30 for girls

Note 1) Patients were included in this analysis if they had pre-dose and weeks 40-48 prolactin observations
2) Improvement is a negative change from pre-dose
3) Improvement could not be calculated from the N-CBRF for patient A3581/D-S who had a 0 score at pre-dose

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Table 34. Responders on the Conduct Problem Subscale of the N-CBRF by Prolactin Levels [ng/mL] (PAP - As Observed): Frequency Tables -(continued)

Response Criteria	Time Period	Responders	N	Above ULN*	Normal	Chi-Square Test p-Value
>= 50% vs < 50%	Weeks 4 to 7	Yes		149 (61.3)	53 (57.6)	0.5358
		No		94 (38.7)	39 (42.4)	
		Total	335	243	92	
	Weeks 8 to 12	Yes		109 (59.6)	86 (58.5)	0.8457
		No		74 (40.4)	61 (41.5)	
		Total	330	183	147	
	Weeks 16 to 24	Yes		75 (59.5)	102 (52.8)	0.2410
		No		51 (40.5)	91 (47.2)	
		Total	319	126	193	
	Weeks 28 to 36	Yes		68 (56.2)	117 (60.0)	0.5049
		No		53 (43.8)	78 (40.0)	
		Total	316	121	195	
	Weeks 40 to 48	Yes		68 (62.4)	145 (59.2)	0.5700
		No		41 (37.6)	100 (40.8)	
		Total	354	109	245	

*ULN: The upper limit of normal for prolactin levels is 18 for boys and 30 for girls

Note 1) Patients were included in this analysis if they had pre-dose and weeks 40-48 prolactin observations
2) Improvement is a negative change from pre-dose
3) Improvement could not be calculated from the N-CBRF for patient A3581/D-S who had a 0 score at pre-dose

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