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Baseline Demographics and Characteristics From a Paliperidone Palmitate Study in Subjects with Recent-Onset Schizophrenia or Schizophreniform Disorder

By Brianne Brown, Larry Alphs, Ibrahim Turkoz, Yong Yue

Introduction

- Early and effective treatment of schizophrenia may slow disease progression and improve overall patient outcomes.[1] In addition, interventions specifically targeting cognitive deficits may prevent chronic disability[2]
- In individuals with first-episode schizophrenia, greater improvements have been reported with long-acting injections vs oral antipsychotics (APs)[3,4]
- The Disease Recovery Evaluation and Modification (DREaM) study is examining whether paliperidone palmitate once-monthly (PP1M) followed by paliperidone palmitate once-every-3-months (PP3M) injections can slow disease progression and possibly modify the course of schizophrenia compared with oral APs in subjects with recent-onset psychosis (schizophrenia or schizophreniform disorder) by tracking changes in cognition, functioning, and intracortical myelin volume and by tracking treatment failures
- Key innovations of the DREaM study include double randomization of matched-control subjects in a delayed-start design. This study design is used to distinguish between a treatment's effect on symptom improvement and potential disease modification[5]
- We describe the baseline demographics and clinical characteristics of early enrollees to the DREaM study

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- These characteristics are compared to those of subjects enrolled in a trial evaluating a similar population: the Recovery After an Initial Schizophrenia Episode (RAISE) study, a multisite, randomized controlled trial in subjects with first-episode psychosis[6]

Methods

Study Designs

DREaM (NCT02431702)

- DREaM is a prospective, matched-control, double-randomized, open-label, flexible-dose study in subjects with recent-onset schizophrenia or schizophreniform disorder that compares disease progression and disease interception following treatment with PP1M/PP3M or oral APs
- Subjects aged 18 to 35 years with a DSM-5 diagnosis of schizophrenia or schizophreniform disorder and first psychotic episode within 2 years of enrollment are eligible
- Participating sites include academic- and community-based clinics both with and without established clinics that specialize in first-episode psychosis
- DREaM includes three treatment phases (Figure 1)

RAISE

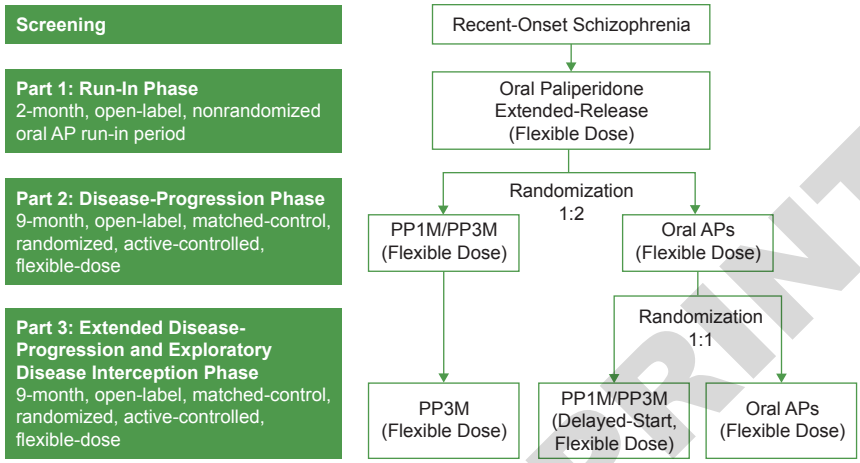
- Subjects were aged 15 to 40 years with a DSM-IV diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, brief psychotic disorder, or psychotic disorder not otherwise specified
- All participants had experienced only one episode of psychosis and had received ⩽6 months of AP medications in their lifetime
- Participating sites included 34 community mental health centers in the United States
- Academic centers or sites with existing first-episode psychosis programs were excluded from participation[6]

DREaM Screening/Baseline Efficacy Assessments

- The following assessments were performed at either screening (visit 1) or baseline (Part 1: visit 2, day 1):
  - Baseline demographics and clinical characteristics
  - MATRICS Consensus Cognitive Battery (MCCB)[7]: Measured key cognitive domains relevant to schizophrenia and related disorders
  - Personal and Social Performance (PSP) scale[8]: Assessed personal and social functioning within the past month

FIGURE 1

DREaM Study Design



Notes: In Part 1, subjects who tolerate paliperidone extended-release but whose clinician finds it inadequately efficacious (per clinical judgment) may be switched to another protocol-specified oral AP: aripiprazole, haloperidol, olanzapine, perphenazine, quetiapine, or risperidone. In Parts 2 and 3, 9-month paliperidone palmitate treatment = PP1M for 4 months (five injections) followed by PP3M for 5 months (two injections).

- Clinical Global Impression of Severity (CGI-S) scale[9]: Rated the severity of the subject's overall clinical condition on a 7-point scale (1 = not ill, 7 = extremely ill)
- Medication Satisfaction Questionnaire (MSQ)[10,11]: Rated self-reported satisfaction with current AP treatment on a 7-point Likert scale (1 = extremely dissatisfied, 7 = extremely satisfied)
- Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS)[12]: An 8-item measure that assesses the severity of mental health symptoms that are important across psychotic disorders, such as delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, negative symptoms, impaired cognition, depression, and mania, on a 5-point scale (0 = none, 4 = present and severe)

Statistical Analyses

- Baseline demographics and clinical characteristics were generated for the DREaM study using descriptive statistics. In some cases where data were available, demographics and clinical characteristics were compared between the DREaM and RAISE studies
- Study comparisons for available data points were carried out using either the chi-squared test for categorical data or the *t*-test for continuous data points

TABLE 1

Baseline Demographics in the DREaM and RAISE Studies

Baseline Characteristic	DREaM: Enrolled Subjects N = 96	RAISE: Final Population[6] N = 404	*P* Value
Age, y, mean (SD)	22.8 (4.0)	23.1 (5.1)	0.512
Sex, male, n (%)	83 (86)	293 (73)	<0.001
Race, n (%)			0.094
White	47 (49)	218 (54)	–
Black	33 (34)	152 (38)	–
Other	15 (16)	34 (8)	–
Missing data	1 (1)	–	–
Ethnicity, n (%)			0.043
Hispanic or Latino	27 (28)	73 (18)	–
Living status, n (%)			<0.001
Independent living	1 (1)	72 (18)	–
Supported or structured	2 (2)	14 (3)	–
With family/friends	86 (90)	287 (71)	–
Homeless/other	7 (7)	31 (8)	
Patient education, n (%)			<0.001
Some college or higher	29 (30)	125 (31)	–
Completed high school	56 (58)	133 (33)	–
Some high or grade school	11 (11)	125 (31)	–
No school or unknown	0	21 (5)	–
Maternal education, n (%)			0.014
Some college or higher	49 (51)	167 (41)	–
Completed high school	30 (31)	111 (27)	–
Some high or grade school	13 (14)	59 (15)	–
No school or unknown	4 (4)	67 (17)	–

Abbreviation: SD, standard deviation.

Results

DREaM vs RAISE Study

- The DREaM study had enrolled 96 subjects as of April 4, 2017
- Baseline demographics in the DREaM and RAISE studies were similar, except for a predominance of males and differences in living status and patient/maternal education in the DREaM study as compared to the RAISE study (Table 1). Some of these differences may be driven by site differences
- The psychiatric history of subjects enrolled in the DREaM and RAISE studies are compared in Table 2. Most characteristics were similar except for the CGI-S rating, suggesting slightly higher disease severity in the DREaM sample at the time of study entry
- The median duration of time since the first episode of psychosis (regardless of treatment status) at screening was 11.1 months. In RAISE the

TABLE 2

Psychiatric History of Subjects Enrolled in DREaM vs RAISE

	DREaM: ENROLLED SUBJECTS N = 96	RAISE: FINAL POPULATION[6] N = 404	*P* VALUE
Current diagnosis			0.414
Schizophrenia, n (%)	77 (80)	214 (53)	–
Schizophreniform disorder, n (%)	19 (20)	67 (17)	–
Other, n (%)	0	123[a]	–
Months since first psychotic episode			
Mean (SD)	12.2 (7.1)	–	NA
Median (range)	11.1 (2–25)	–	–
CGI-S			0.002
Mean (SD)	4.4 (1.0)	4.1 (0.8)	–
Range	2–7	–	–
Total number of prior hospitalizations			NA
Mean (SD)	1.2 (1.2)	–	–
Range	0–6	–	–
Number of prior hospitalizations, n (%)			0.145
0	28 (29)	88 (22)	–
1	33 (34)	181 (45)	–
2	21 (22)	69 (17)	–
⩾3	12 (13)	64 (16)	–
Missing data	2 (2)	2 (0.5)	–
Cumulative substance history, n (%)			NA
<6 months	2 (2)	–	–
6–12 months	1 (1)	–	–
>12 months	59 (61)	–	–
Missing data, n (%)	34 (35)	–	–

Note: [a]A total of 123 subjects in the RAISE study had psychotic diagnoses other than schizophrenia or schizophreniform disorder.
Abbreviation: NA, not applicable.

median duration of untreated psychosis was approximately 17 months, suggesting that these subjects took longer to begin treatment[6]
- The history of AP exposure and current AP treatment at screening for subjects enrolled in DREaM is shown in Table 3
- In comparison, all subjects in RAISE were required to have <6 months of exposure, and 83% were prescribed one or more APs at baseline[6]

Additional Clinical Characteristics of DREaM

- Most subjects enrolled in DREaM (80%) had a CGI-S score of ⩾4, which is indicative of a population that is moderately to extremely ill (Figure 2)
- At baseline, there was a wide range of satisfaction with current AP medication, with the most common response being "somewhat satisfied" (27%; Figure 3)

TABLE 3

AP Treatment at Screening for DREaM Subjects

	DREaM SUBJECTS N = 96
Duration of prior AP exposure, n (%)	
<6 months	48 (50)
6–12 months	16 (17)
>12 months	23 (24)
Missing data, n (%)	9 (9)
Current AP treatment at screening,[a] n (%)	
Risperidone	25 (26)
Paliperidone	18 (19)
Olanzapine	12 (13)
Haloperidol	8 (8)
Quetiapine	8 (8)
Aripiprazole	6 (6)
Lurasidone hydrochloride	3 (3)
Other	3 (3)
Loxapine	1 (1)
Ziprasidone hydrochloride	1 (1)
Not assigned[b]	22 (23)

Notes: [a]Drugs selected if they are used on the reference start date or 2 weeks before it. [b]Subjects who were not assigned to any medications.

FIGURE 2

Baseline CGI-S Scale

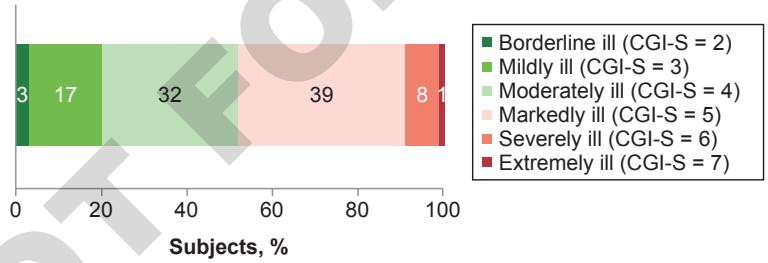
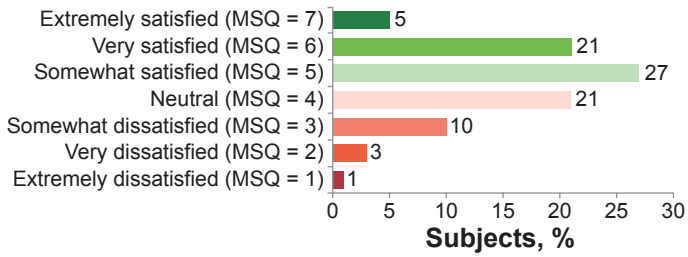


FIGURE 3

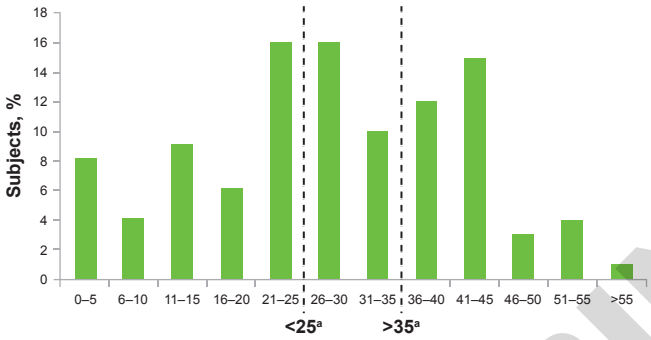
Medical Satisfaction as Assessed Using the MSQ at Screening (N = 96)



Note: 11 subjects were not assessed.

FIGURE 4

Cognition as Assessed Using the MCCB at Screening (N = 93)



MCCB N = 96	Overall Composite Score	Neurocognitive Composite Score	Speed of Processing	Attention/ Vigilance	Working Memory	Verbal Learning	Reasoning and Problem Solving	Social Cognition
Mean (SD)	28.2 (13.9)	28.9 (13.3)	31.5 (13.7)	34.7 (12.0)	38.2 (12.2)	38.2 (10.1)	38.5 (10.5)	41.0 (12.6)

Notes: [a]Cutoff for randomization factors. A higher score indicates better performance. A score of <35 indicates impairment, whereas 35–60 is within the average range.

- The mean ± SD MCCB score is 28.2 ± 13.9; 42% of subjects had a score of ⩽25 (Figure 4)
- The screening mean ± SD PSP scale score is 49.5 ± 14.6 (range, 5–80). Most subjects had a score of 31 to 70 (86%), indicating a moderate degree of social dysfunction at baseline (Figure 5)

FIGURE 5

Baseline PSP Scale Total Scores (A) and Domain Scores (B)

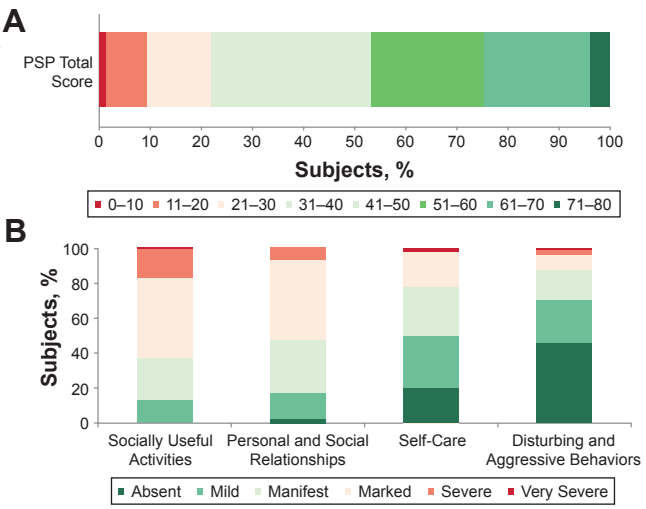
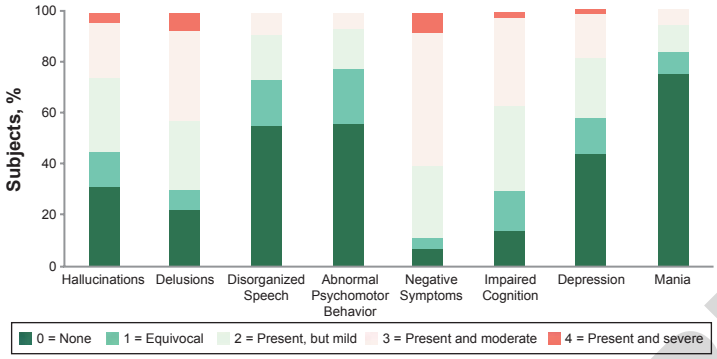


FIGURE 6

Frequency of CRDPSS Item Ratings at Screening



CRDPSS N = 96	Hallucinations	Delusions	Disorganized Speech	Abnormal Psychomotor Behavior	Negative Symptoms	Impaired Cognition	Depression	Mania
Mean (SD)	1.5 (1.3)	2.0 (1.3)	0.8 (1.0)	0.7 (1.0)	2.5 (1.0)	2.0 (1.1)	1.2 (1.2)	0.4 (0.8)

Note: Items are rated on a 5-point scale where 0 = none and 4 = present and severe.

- The most severe CRDPSS ratings were observed in delusions, negative symptoms, and impaired cognition (Figure 6)

Limitations

- Between the two studies, there were differences in both inclusion criteria and research site types
- The DREaM study sample presented here represents only one-third of the planned enrollment. Thus, it may not reflect the full population to be studied

Discussion

- Most subjects with recent-onset psychosis enrolled in the DREaM study had at least one prior hospitalization, a history of substance use, a CGI-S score of ⩾4, and a moderate degree of social dysfunction
- With a few exceptions, the baseline demographics and characteristics of subjects in the DREaM study appear similar to those reported in the RAISE study in subjects with first-episode psychosis receiving treatment at US community mental health centers
- The DREaM study population's baseline characteristics and clinical data represent those of a population recently diagnosed with schizophrenia and will be used to match subjects in anticipation of randomization for Parts 2 and 3 of the study ✤

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Disclosures

B. Brown, L. Alphs, and Y. Yue are employees of Janssen Scientific Affairs, LLC, and are Johnson & Johnson stockholders. I. Turkoz is an employee of Janssen Research and Development, LLC, and is a Johnson & Johnson stockholder.

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