Invega Sustenna®
(Paliperidone Palmitate 1-Month Prolonged-Release Injectable Suspension)
Comparative Efficacy (PRIDE Study)

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Overview[1]

The Paliperidone Palmitate Research in Demonstrating Effectiveness (PRIDE) study was a 15-month, US, prospective, randomized, open-label, event monitoring board-blinded, multicenter, comparative study of PP1M vs oAPs on time to first treatment failure in patients with schizophrenia recently released from incarceration

(N=444)

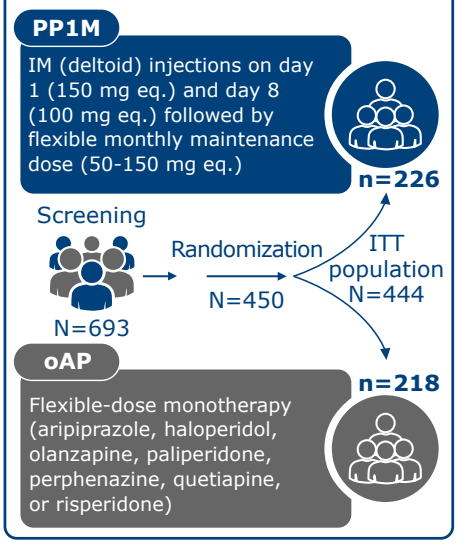
Inclusion Criteria[1]

- Adult patients (age, 18-65 years)
- Placed in custody ≥2 times in previous 2 years, with ≥1 event leading to incarceration
- Custodial release within 90 days of screening

Exclusion Criteria[1]

- Clozapine/injectable antipsychotic drug use (within 3 months of screening)
- IV drug abuse (within 3 months of screening) or opioid dependence disorder

Study Design[1]



Efficacy Outcomes[1]

- Median time to first treatment failure was significantly longer in the PP1M vs oAP group (416 vs 226 days; *P*=0.011)
- Fewer patients reported treatment failure in PP1M vs oAP group (39.8% vs 53.7%)
- Risk of first psychiatric hospitalization or arrest/incarceration was higher in oAP vs PP1M group (1.43×; 95% CI, 1.09-1.88)

Safety Outcomes (PP1M vs oAP)[1]

TEAEs >10% in either arm

- Injection site pain: 18.6% vs 0%
- Insomnia: 16.8% vs 11.5%
- Weight gain: 11.9% vs 6.0%
- Akathisia: 11.1% vs 6.9%
- Anxiety: 10.6% vs 7.3%

Other Safety Outcomes

- Weight gain (≥7%): 32.4% vs 14.4%
- Prolactin-related TEAEs: 23.5% vs 4.1%
- TEAEs leading to drug discontinuation: 11.9% vs 7.8%

Results of Post Hoc Analyses

- The median time to first treatment failure and to first psychiatric hospitalization or arrest/incarceration in the **Black/African American patient subgroup** was greater in the PP1M vs oAP group[2]
- In the **substance abuse and non-abuse cohorts,** a higher risk of treatment failure was observed with oAP vs PP1M therapy[3]
- The **mean cumulative function of number of treatment failures** and **institutionalizations** was significantly lower in the PP1M vs oAP group[4]
- The **risk of treatment failure** was lower with PP1M vs A-oAP, C-oAP, and PAL+RIS[5]

Doses of paliperidone palmitate extended-release injectable suspension may be expressed in milligram equivalents of paliperidone (active moiety) or milligrams of paliperidone palmitate. The conversion factor from mg eq. to mg is 1.56.

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mg	39	78	117	156	234
mg eq.	25	50	75	100	150

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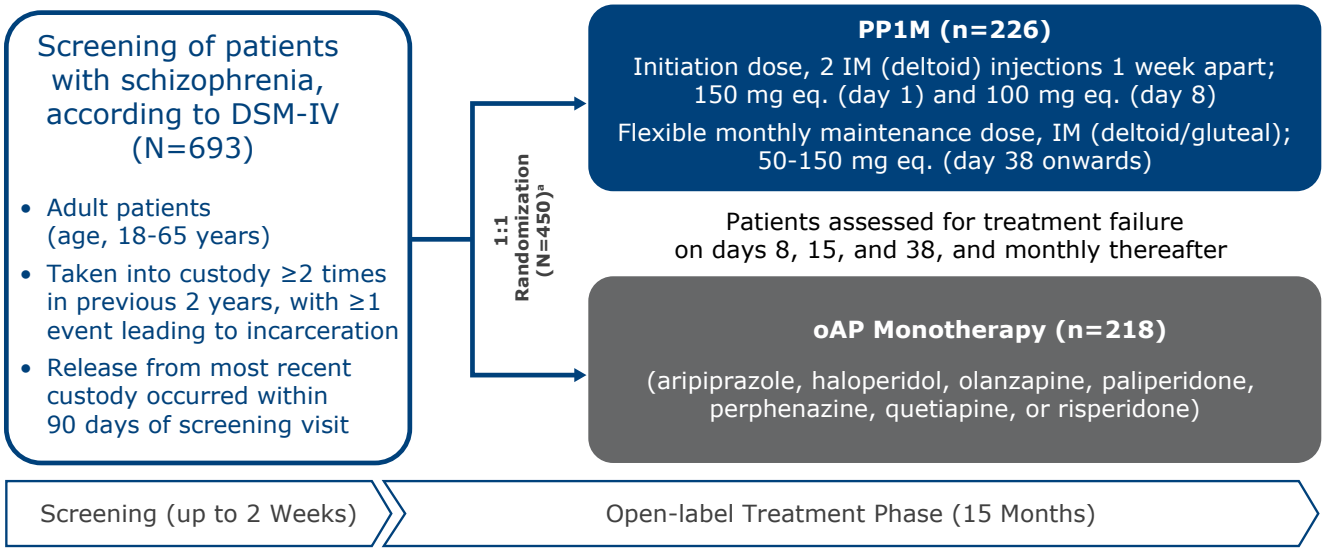
PRIDE was a 15-month, prospective, randomized, open-label, event-monitoring board-blinded study in a community sample of patients from nontraditional locations (ie, homeless shelters, soup kitchens, jail-release or diversion programs) with schizophrenia, recently released from incarceration, receiving PP1M or oAPs daily.[1]



[a]**Clinician's and patient's joint review of available oAP for acceptability**

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Inclusion Criteria[1]	**Exclusion Criteria**[1]
• Adult patients (age, 18-65 years) with schizophrenia per DSM-IV • Placed in custody ≥2 times in previous 2 years, with ≥1 event leading to incarceration • Release from most recent custody occurred within 90 days of screening	• Use of either clozapine or an injectable antipsychotic within 3 months or 2 injection cycles of screening, respectively • Substance abuse was not exclusionary; however, patients abusing IV drugs within 3 months of screening or with an opiate dependence disorder were excluded

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Primary Efficacy Endpoint[1]

- Time to first treatment failure defined as:
  - arrest or incarceration
  - psychiatric hospitalization
  - suicide
  - treatment discontinuation due to inadequate efficacy, safety, or tolerability
  - treatment supplementation due to inadequate efficacy, or
  - increase in level of psychiatric services to prevent imminent psychiatric hospitalization

Secondary Efficacy Endpoints[1]

- Time to first psychiatric hospitalization or arrest/incarceration
- Change in PSP scores
- Change in CGI-S score

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- Demographics and baseline characteristics were similar between treatment groups.[1]

Baseline Characteristics	PP1M (n=226)	oAP (n=218)
Age, years, mean (SD)	37.7 (10.6)	38.6 (10.4)
Male, n (%)	193 (85.4)	190 (87.2)
Race, n (%)		
White	73 (32.3)	74 (34.1)[a]
Black/African American	145 (64.2)	130 (59.9)[a]
Others	8 (3.5)	13 (6.0)[a]
Time since release from last incarceration, mean, days	38.9	45.7[a]
Concurrent substance abuse, n (%)	130 (57.5)	134 (61.5)
Number of psychiatric hospitalizations, mean	7.3[b]	5.7[c]
PSP total score, mean (SD)	54.8 (12.8)	55.0 (12.7)[d]
CGI-S score, mean (SD)	3.8 (0.8)	3.9 (0.7)[a]

[a]n=217; [b]n=176; [c]n=170; [d]n=215.

- The mean exposure to PP1M was 266.2 days and to oAP was 271.5 days.[1]

Mean Drug Doses[1]

	PP1M	HAL	PER	ARI	OLA	QUE	PAL	RIS
Mean dose, mg	116.2[a] (n=226)	7.7[b] (n=11)	14.4[b] (n=18)	16.6[b] (n=25)	13.2[b] (n=31)	335.9[b] (n=24)	6.4[b] (n=43)	3.4[b] (n=30)

[a]Dose per injection records (116.2 mg eq. paliperidone = 181.3 mg paliperidone palmitate); [b]Dose per refill records.

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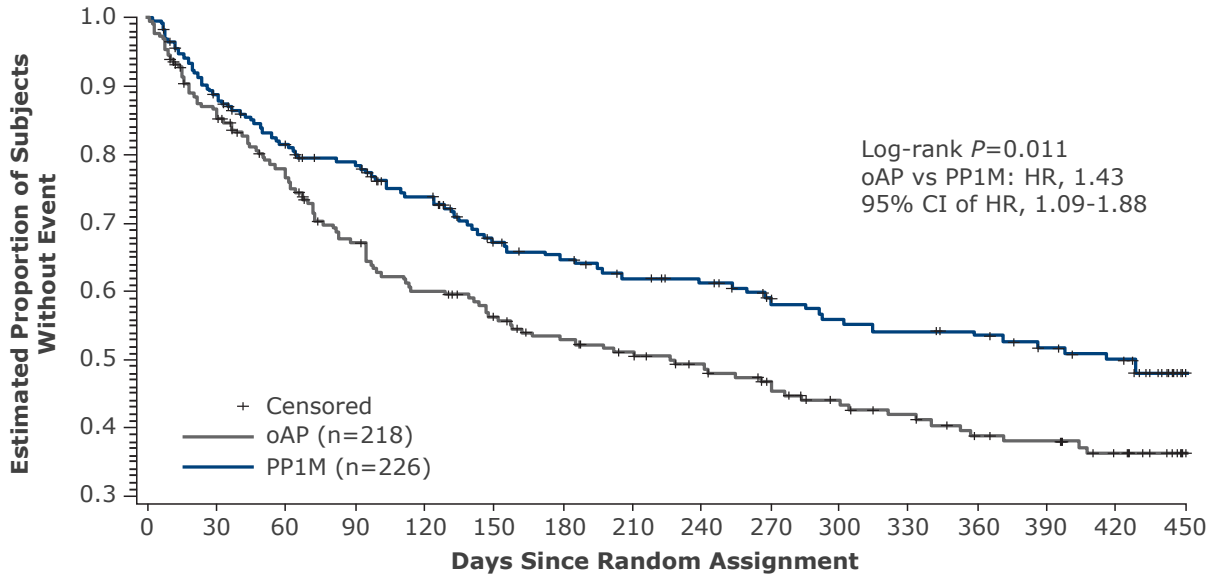
- The median time to first treatment failure was significantly longer for PP1M vs oAP (416 vs 226 days; *P*=0.011).[1]

Time to First Treatment Failure[1]



No. of subjects at risk

oAP	218	183	152	126	112	102	92	86	79	71	61	58	49	47	41	29
PP1M	226	190	162	148	128	107	100	92	88	76	70	68	65	60	56	31

- Treatment failure was reported in 68.7% of patients overall, and in 39.8% vs 53.7% of patients in the PP1M vs oAP group, respectively.[1]
- Risk of treatment failure was 1.43 times higher in the oAP vs PP1M group (95% CI, 1.09-1.88).[1]

Reasons for First Treatment Failure

Reasons for First Treatment Failure

Reasons for First Treatment Failure, n (%)[1]	PP1M (n=226)	oAP (n=218)
Arrest/incarceration	48 (21.2)	64 (29.4)
Psychiatric hospitalization	18 (8.0)	26 (11.9)
Discontinuation of antipsychotic treatment due to safety or tolerability	15 (6.6)	8 (3.7)
Treatment supplementation with another antipsychotic due to inadequate efficacy	5 (2.2)	6 (2.8)
Discontinuation of antipsychotic treatment due to inadequate efficacy	1 (0.4)	9 (4.1)
Increase in level of psychiatric services to prevent imminent psychiatric hospitalization	3 (1.3)	4 (1.8)

oAP, oral antipsychotic; PP1M, paliperidone palmitate 1-month.

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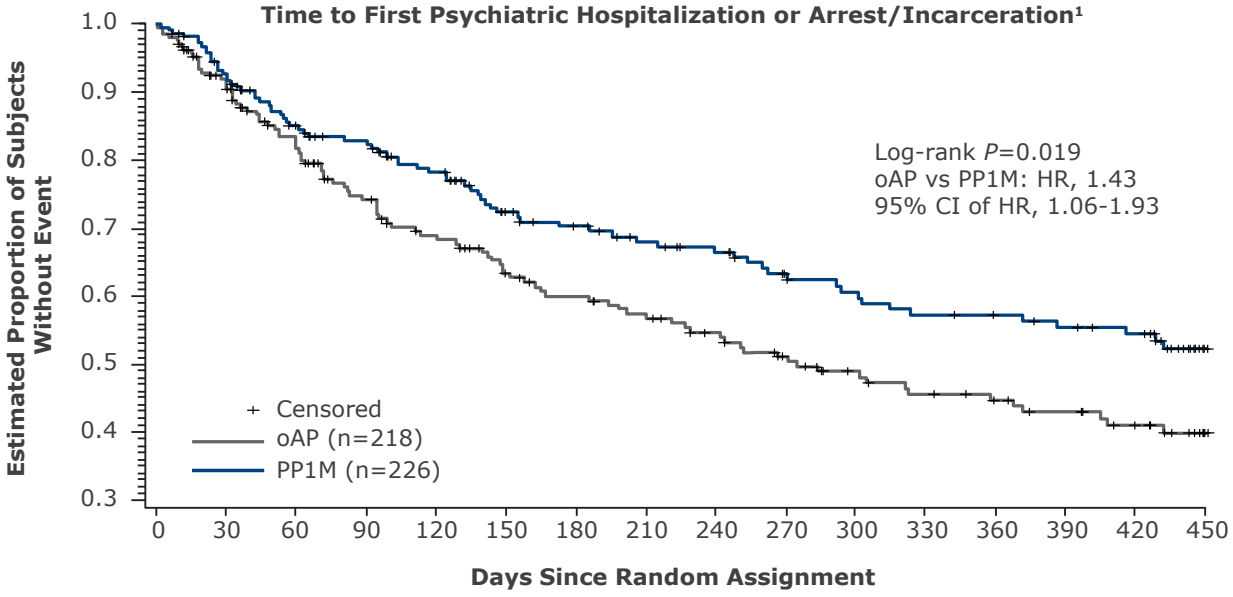
- A significantly longer time to first psychiatric hospitalization or arrest/incarceration was observed with PP1M vs oAP (*P*=0.019).[1]
  - The risk of first psychiatric hospitalization or arrest/incarceration was 1.43 times higher in the oAP vs PP1M group (95% CI, 1.06-1.93).



No. of subjects at risk

oAP	218	187	151	127	114	101	92	86	78	69	61	56	52	47	41	29
PP1M	226	192	163	148	128	108	100	92	87	75	70	66	64	61	58	33

- No significant between-group differences were observed in mean change in PSP total scores (least squares mean [SE] difference=0.39 [0.98]) and CGI-S scores (least squares mean [SE] difference= -0.06 [0.05]).[1]

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Treatment-Emergent Adverse Events[1]

- **Most common AEs** reported were injection site pain, insomnia, weight gain, akathisia, and anxiety in the PP1M group; and insomnia, headache, dry mouth, anxiety, and sedation in the oAP group.
- **Serious TEAEs** were reported in 17.3% of patients receiving PP1M and 21.6% of patients receiving oAP.
- **TEAEs leading to drug discontinuation** occurred in 11.9% of patients receiving PP1M and 7.8% of patients receiving oAP.
- A **treatment-emergent prolactin-related AE** was reported in 23.5% (n=53) of patients receiving PP1M and 4.1% (n=9) of patients receiving oAP.
- Rates of **EPS-related TEAEs** for the PP1M and oAP groups, respectively, were as follows: akathisia (11.1% vs 6.9%), dyskinesia (2.7% vs 1.4%), dystonia (2.2% vs 2.8%), and parkinsonism (1.8%, each).
- **Weight gain increase** ≥7% was observed in 32.4% of PP1M and 14.4% of oAP patients.

Summary of TEAEs in >10% of Patients

Summary of TEAEs in >10% of Patients[1]

TEAEs, n (%)	PP1M (n=226)	oAP (n=218)
Injection site pain	42 (18.6)	0
Insomnia	38 (16.8)	25 (11.5)
Weight gain	27 (11.9)	13 (6.0)
Akathisia	25 (11.1)	15 (6.9)
Anxiety	24 (10.6)	16 (7.3)

oAP, oral antipsychotic; PP1M, paliperidone palmitate 1-month; TEAE, treatment-emergent adverse event.

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Bell Lynum et al (2018)[2]

Objective: To evaluate the efficacy of PP1M vs oAP in delaying time to first relapse in Black/African American patients (N=275)

Parameter	PP1M vs oAP
Median time to first treatment failure →	**NR (>450 days) vs 270 days** HR, 1.39 (95% CI, 0.97-1.99); *P*=0.075
Median time to first psychiatric hospitalization or arrest/incarceration →	**NR (>450 days) vs 304 days** HR, 1.49 (95% CI, 1.01-2.19); *P*=0.043

Safety results were not reported

The median time to treatment failure and to first psychiatric hospitalization or arrest/incarceration were greater in the PP1M vs oAP group.[2]

Starr et al (2018)[3]

Objective: To evaluate the impact of substance abuse on treatment failure with PP1M vs oAP

Risk of Treatment Failure (PP1M vs oAP)

Substance Abuse Cohort	Nonabuse Cohort
56.2% vs 64.2% HR, 1.48; *P*=0.016	36.5% vs 53.6% HR, 1.77; *P*=0.015

Greater treatment effects were seen with PP1M compared with oAP in both the substance abuse and nonabuse cohorts. The effect of PP1M vs oAP was attenuated in the substance abuse cohort.

Most frequently reported **TEAEs** (**≥20%** in either group and cohort): weight gain, EPS-related TEAEs, prolactin-related TEAEs, injection site pain, and insomnia.

Median Time to Key Events, Days	Substance Abuse Cohort	Nonabuse Cohort
Treatment failure	291 vs 186	>450 vs 284
Psychiatric hospitalization or arrest/incarceration	371 vs 317	>450 vs 371

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Alphs et al (2016)[4]

Objective: To compare the mean cumulative function of treatment failure and safety in PP1M vs oAP group

Parameter	PP1M vs oAP
Mean cumulative function of treatment failure	1.02 vs 1.50 (*P*=0.007)
Mean cumulative function of institutionalization[a]	0.82 vs 1.27 (*P*=0.005)
TEAEs	86.3% vs 81.7%
TEAE-related treatment discontinuation	12.4% vs 8.7%

The mean cumulative function of treatment failure and institutionalization was significantly lower in the PP1M vs oAP group.

[a]Arrests, incarcerations, or psychiatric hospitalizations.

Kim et al (2016)[5]

Objective: To evaluate the efficacy and safety of PP1M vs 3 oAP subgroups

Risk of Treatment Failure

- **C-oAP[a] vs PP1M:** 34% higher HR, 1.34; *P*=0.262
- **A-oAP[b] vs PP1M:** 41% higher HR, 1.41; *P*=0.019
- **PAL+RIS vs PP1M:** 39% higher HR, 1.39; *P*=0.071

The risk of treatment failure was lower with PP1M vs A-oAP, C-oAP, and PAL+RIS.

Most common **TEAEs in ≥10**% of subjects in either group, were injection site pain, insomnia, weight gain, akathisia, and anxiety (similar to PRIDE study).

TEAE Category	PP1M	oAP Groups
≥7% weight increase	32.4%	11.4% (C-oAP) 14.9% (A-oAP) 16.0% (PAL+RIS)
EPS-related	23.9%	45.7% (C-oAP) 13.7% (A-oAP) 10.6% (PAL+RIS)
Prolactin-related	23.5%	5.7% (C-oAP) 3.8% (A-oAP) 3.5% (PAL+RIS)

[a]HAL and PER; [b]ARI, OLA, QUE, PAL, and RIS.

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AE	Adverse event	**oAP**	Oral antipsychotic
A-oAP	Atypical oAP	**OLA**	Olanzapine
ARI	Aripiprazole	**PAL**	Paliperidone
CGI-S	Clinical Global Impressions- Severity of Illness Scale	**PAL+RIS**	Oral paliperidone and risperidone
CI	Confidence interval	**PER**	Perphenazine
C-oAP	Conventional oAP	**PP1M**	Paliperidone palmitate 1-month
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th edition	**PRIDE**	Paliperidone Palmitate Research In Demonstrating Effectiveness
EPS	Extrapyramidal symptom	**PSP**	Personal and Social Performance Scale
HAL	Haloperidol	**QUE**	Quetiapine
HR	Hazard ratio	**RIS**	Risperidone
IM	Intramuscular	**SD**	Standard deviation
ITT	Intention-to-treat	**SE**	Standard error
IV	Intravenous	**TEAE**	Treatment-emergent AE
NR	Not reached	**US**	United Sates

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A literature search of MEDLINE® (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 26 May 2020.

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1. Alphs L, Benson C, Cheshire-Kinney K, et al. Real-world outcomes of paliperidone palmitate compared to daily oral antipsychotic therapy in schizophrenia: a randomized, open-label, review board-blinded 15-month study. *J Clin Psychiatry*. 2015;76:554-561.
2. Bell Lynum KS, Gogate J, Kim E. Treatment effect of once-monthly paliperidone palmitate compared with oral antipsychotics in African American patients diagnosed with schizophrenia with a history of criminal justice system involvement. Poster presented at: US Psych Congress; October 25-28, 2018; Orlando, FL.
3. Starr H, Bermak J, Mao L, et al. Comparison of long-acting and oral antipsychotic treatment effects in patients with schizophrenia, comorbid substance abuse, and a history of recent incarceration: an exploratory analysis of the PRIDE study. *Schizophr Res*. 2018;194:39-46.
4. Alphs L, Mao L, Lynn Starr H, et al. A pragmatic analysis comparing once-monthly paliperidone palmitate versus daily oral antipsychotic treatment in patients with schizophrenia. *Schizophr Res*. 2016;170:259-264.
5. Kim E, Correll CU, Mao L, et al. Once-monthly paliperidone palmitate compared with conventional and atypical daily oral antipsychotic treatment in patients with schizophrenia. *CNS Spectr*. 2016;21:466-477.