Clinician's Guide to Prescribing Depot Antipsychotics
Learning Objectives

• Explain the benefits and risks of depot antipsychotics

• Optimize the utilization of individual depot antipsychotics
Pretest Question 1

Sarah is a 24-year-old patient with schizophrenia. She has a history of treatment non-adherence due to an aversion to swallowing pills. Which of the following antipsychotics is currently available in a long-acting injectable formulation?

1. Asenapine
2. Olanzapine
3. Iloperidone
4. 1 and 2 only
5. 2 and 3 only
Pretest Question 2

Mark is a 41-year-old patient with schizoaffective disorder. He has been taking the depot formulation of paliperidone (Invega Sustenna, 234 mg) for the past 2 years. Unfortunately, Mark has missed his last 2 appointments and consequently has not been administered antipsychotic treatment for approximately 8 weeks. How should paliperidone palmitate be reinitiated in this patient?

1. Initiate daily oral paliperidone followed by a 234-mg paliperidone injection 1 week later

2. Initiate patient with a 156-mg paliperidone palmitate injection followed by another 156-mg injection 1 week later

3. Immediately resume the previously established 234-mg paliperidone palmitate injection
Pretest Question 3

Ike is a 61-year-old patient with schizophrenia who is currently only partially adherent to his daily oral haloperidol treatment (5 mg/day). He has agreed to try the depot formulation of haloperidol (haloperidol decanoate). In order to achieve optimal plasma levels of haloperidol, the monthly injected dose of haloperidol decanoate should be:

1. 50 mg/month
2. 100 mg/month
3. 200 mg/month
Why Use Long-Acting Injectable Antipsychotics?

**Advantages**

- Assured medication delivery and continuous antipsychotic coverage
- No need to remember to take medication every day
- Clinician can be immediately notified of non-adherence
- Drug remains in system for weeks after a missed dose
- Reduce relapse frequency and rehospitalization rates
- Avoidance of first-pass metabolism, so there is a better relationship between dose and blood level of drug
- Lower peak plasma level may be associated with reduced side effects
- Peak plasma level occurs less often, so may lead to reduced side effects

**Disadvantages**

- Cost/insurance coverage
- Oral to LAI conversion
- Perceived stigma
- Negative perception/stigma
- Lack of personnel to administer depot

Impact on Clinical Decisions

• Oral antipsychotics
  – Unknown compliance may prevent evaluation of medication effectiveness
    • Change medication?
    • Increase dose?
    • Augment?

• Long-acting injectables
  – Known adherence allows for evaluation of medication effectiveness
  – Missed dose can trigger intervention
  – Patient–clinician interaction

Depot Injections Are Associated With a 50-65% Lower Risk of Rehospitalization Than Their Oral Counterparts

Do Depot Antipsychotics Reduce Relapse Risk? Meta-analysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Depot Events</th>
<th>Total</th>
<th>Oral Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arango 2005</td>
<td>10</td>
<td>26</td>
<td>6</td>
<td>20</td>
<td>5.2%</td>
<td>1.28 [0.56, 2.93]</td>
</tr>
<tr>
<td>Barnes 1983</td>
<td>3</td>
<td>19</td>
<td>3</td>
<td>17</td>
<td>1.9%</td>
<td>0.89 [0.21, 3.85]</td>
</tr>
<tr>
<td>Del Guidice 1975</td>
<td>21</td>
<td>27</td>
<td>30</td>
<td>31</td>
<td>22.8%</td>
<td>0.80 [0.65, 0.99]</td>
</tr>
<tr>
<td>Falloon 1978</td>
<td>8</td>
<td>20</td>
<td>5</td>
<td>24</td>
<td>4.2%</td>
<td>1.92 [0.74, 4.95]</td>
</tr>
<tr>
<td>Gaebel 2010</td>
<td>54</td>
<td>355</td>
<td>102</td>
<td>355</td>
<td>18.6%</td>
<td>0.53 [0.39, 0.71]</td>
</tr>
<tr>
<td>Hogarty 1979</td>
<td>22</td>
<td>55</td>
<td>32</td>
<td>50</td>
<td>14.8%</td>
<td>0.63 [0.43, 0.92]</td>
</tr>
<tr>
<td>Li 1996</td>
<td>32</td>
<td>155</td>
<td>52</td>
<td>137</td>
<td>15.1%</td>
<td>0.54 [0.37, 0.79]</td>
</tr>
<tr>
<td>Potapov 2008</td>
<td>4</td>
<td>20</td>
<td>8</td>
<td>20</td>
<td>3.6%</td>
<td>0.50 [0.18, 1.40]</td>
</tr>
<tr>
<td>Rifkin 1977</td>
<td>2</td>
<td>23</td>
<td>3</td>
<td>28</td>
<td>1.4%</td>
<td>0.81 [0.15, 4.45]</td>
</tr>
<tr>
<td>Schooler 1979</td>
<td>26</td>
<td>143</td>
<td>35</td>
<td>147</td>
<td>12.4%</td>
<td>0.76 [0.49, 1.20]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>843</strong></td>
<td><strong>829</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>0.70 [0.57, 0.87]</strong></td>
</tr>
</tbody>
</table>

Total events: 182, 276

Heterogeneity: $\tau^2 = 0.04; \chi^2 = 15.35, df = 9 (P = 0.08); I^2 = 41\%$

Test for overall effect: $Z = 3.32 (P = 0.0009)$

Conclusions: relative and absolute relapse risk reductions of 30% and 10%, respectively (RR 0.70, CI 0.57-0.87, NNT 10, CI 6-25, $P=0.0009$)

Leucht C et al. Schizophr Res 2011;in press.
Not All Studies Show Superiority of Depot Antipsychotics

# Relapse Risk: Oral vs. Depot Antipsychotics in Mirror Image Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Tx Duration</th>
<th># of Hosp Days: Oral</th>
<th># of Hosp Days: Depot</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denham &amp; Anderson (1973)</td>
<td>103</td>
<td>12-40 mos</td>
<td>8,719</td>
<td>1,335</td>
<td>$10^{-15}$</td>
</tr>
<tr>
<td>Devito et al. (1978)</td>
<td>122</td>
<td>1 yr</td>
<td>3,329</td>
<td>314</td>
<td>$10^{-2}$</td>
</tr>
<tr>
<td>Freeman (1980)</td>
<td>143</td>
<td>12 yrs</td>
<td>19,510</td>
<td>4,376</td>
<td>$10^{-25}$</td>
</tr>
<tr>
<td>Gottfries &amp; Green (1974)</td>
<td>36</td>
<td>2-6 yrs</td>
<td>12,390</td>
<td>2,940</td>
<td>$10^{-4}$</td>
</tr>
<tr>
<td>Marriott &amp; Hiep (1976)</td>
<td>131</td>
<td>$\geq$ 1 yr</td>
<td>12,434</td>
<td>5,619</td>
<td>$10^{-5}$</td>
</tr>
<tr>
<td>Tegler &amp; Lehmann (1981)</td>
<td>78</td>
<td>5 yrs</td>
<td>19,110</td>
<td>3,276</td>
<td>$10^{-5}$</td>
</tr>
</tbody>
</table>
CONVENTIONAL DEPOTS

- Fluphenazine decanoate (2-3 wks)
- Haloperidol decanoate (4 wks)
- Pipothiazine (4 wks)
- Flupenthixol* (1-4 wks)
- Zuclopenthixol* (2-4 wks)

* Not available in the United States
Fluphenazine Decanoate
Haloperidol Decanoate
Ester Depot Disposition

Injection → Esterified drug in oil

Esterified drug in oil → Esterified drug in plasma

Active drug → Metabolism to active & inactive metabolites

Metabolism to active & inactive metabolites

Renal & biliary excretion → CSF

CSF → Receptor binding

Receptor binding → Multicompartment tissue binding

Multicompartment tissue binding
## Preparations and Basic Kinetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vehicle</th>
<th>Dosage</th>
<th>$T_{\text{max}}$ (days)</th>
<th>$T_{1/2}$ (days) Single Dose</th>
<th>$T_{1/2}$ (days) Multiple Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluphenazine decanoate</td>
<td>Sesame oil</td>
<td>12.5-100 mg/2-6 weeks</td>
<td>0.3-1.5</td>
<td>6-9</td>
<td>14</td>
</tr>
<tr>
<td>Haloperidol decanoate</td>
<td>Sesame oil</td>
<td>25-400 mg/4 weeks</td>
<td>3-9</td>
<td>?</td>
<td>21</td>
</tr>
</tbody>
</table>

Understanding Depot Kinetics

• Rate-limiting step for drugs is slow absorption from the injection site

• The observed terminal phase decline in plasma levels of fluphenazine decanoate corresponds to a half-life of 8-14 days rather than the elimination half-life of 15-24 hours

• For haloperidol decanoate, the observed terminal half-life is 19-21 days rather than 15-24 hours

• This pharmacokinetic action is called **flip-flop kinetics** and is the basis for understanding appropriate dosing with the older depot medications

Fluphenazine Decanoate: Single-Dose Pharmacokinetics

Fluphenazine Decanoate: Chronic Dosing (25 mg/2 wks)

Fig. 1. Mean FPZ dec concentrations (ng/ml) over 2 week period in serum of nine patients treated for at least 3 months with 1 ml i.m. (25 mg/ml) every 2 weeks.

Fluphenazine Decanoate: Chronic Dosing (25 mg/2 wks)

Flu Level (ng/mL)

Week

Baseline

Fluphenazine Decanoate: Conversion From Oral

- Formulas are less reliable than haloperidol oral depot
- Schooler (1976): 10 mg/day oral = 12.5 mg IM q 3 wks
- Ereshefsky (1985): 1.6 times the oral daily dose in mg/day as a WEEKLY injection for the first 4-6 weeks, then conversion to less frequent intervals

Fluphenazine Decanoate: Chronic Dosing (50 mg/week)

Probability Curves of Response and Disabling Side Effects by Plasma Fluphenazine Level

Fluphenazine Decanoate: Extended Interval Dosing

Percentage of Schizophrenia Outpatients Who Remained Clinically Stable While Receiving 25 mg Every 2 Weeks (N=25) or Every 6 Weeks (N=25)

## Preparations and Basic Kinetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vehicle</th>
<th>Dosage</th>
<th>$T_{\text{max}}$ (days)</th>
<th>$T_{1/2}$ (days) Single Dose</th>
<th>$T_{1/2}$ (days) Multiple Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluphenazine decanoate</td>
<td>Sesame oil</td>
<td>12.5-100 mg/2-6 weeks</td>
<td>0.3-1.5</td>
<td>6-9</td>
<td>14</td>
</tr>
<tr>
<td>Haloperidol decanoate</td>
<td>Sesame oil</td>
<td>25-400 mg/4 weeks</td>
<td>3-9</td>
<td>?</td>
<td>21</td>
</tr>
</tbody>
</table>

Haloperidol Decanoate: Concentration vs. Time

Mean monthly dose = 243 mg

Haloperidol Decanoate: Conversion From Oral

- Studies using 10, 20, and 30 times the oral daily dose have been performed

- 20 times the oral daily dose provided optimum plasma concentrations **DURING THE EARLY PHASE OF TREATMENT**
  - Oral haloperidol bioavailability is 65% (range 60-70%)
  - Example: patient on 10 mg/day x 30 days x 65% = 195 mg/month ~ 20 times oral daily dose

- Over time, may be able to decrease the maintenance dose once steady state is reached

Haloperidol Decanoate: Loading Strategies

• Starting with 20 times the estimated oral dose for the first month (divided into 2 injections) was superior to lower depot doses, even with oral supplementation

• 21 patients treated with oral haloperidol for 6 weeks were switched to decanoate 100 mg weekly for 4 weeks, then 100 mg every 2 weeks and then every 4 weeks
  – All patients completed the conversion trial during the first 4 weeks without any problems or adverse side effects
  – By week 3, mean plasma haloperidol concentrations from depot were comparable to 10-mg oral haloperidol (7.95 ± 4.94 ng/mL vs. 7.79 ± 4.79 ng/mL); steady state conditions for the decanoate were achieved by the fourth week

ATYPICAL DEPOTS

Risperidone (Risperdal® Consta®)

Paliperidone palmitate (Invega® Sustenna®)

Olanzapine pamoate (Zyprexa® Relprevv®)
Risperidone Compared to Paliperidone

- Similar pharmacology for risperidone and 9-OH risperidone, but very different kinetics between Consta and Sustenna

- Both recommend that patient have a test dose of risperidone (for either Consta or Sustenna) or paliperidone (OK for Sustenna) if never received before
Risperdal Consta: Formulation and Medication Release

Risperidone

CROSS-LINKED chains

Glycolide

Lactide

Microsphere w/ risperidone

Aqueous DILUENT and injection

Natural exposure to \( \text{H}_2\text{O} \) in the body

\( \text{CO}_2 + \text{H}_2\text{O} \)

CLINICAL ACTIVITY

Risperidone
Risperidone Microspheres

All Consta injections are 2 mL regardless of dose
Lower Peak Plasma Levels vs. Oral

Focused sampling Oral (n = 21)

Focused sampling Consta (n = 21)

Focused sampling from 4th injection

Plasma risperidone + 9-hydroxyrisperidone (ng/mL)

Day

Injection #

Risperdal Consta 25 mg every 2 weeks

12-Week Study: Trial Design

Oral supplementation: 3 weeks

1-week up-titration with risperidone oral (to 4 mg)

1-week down-titration from previous neuroleptic

Oral supplementation:
- Placebo
- 25 mg
- 50 mg
- 75 mg

Blood Levels After Single 25-mg Dose

25-mg dose, N = 14

Data on file, Janssen.
Plasma Levels: Steady State

\[ T_{\text{max}}: \sim 3-4 \text{ weeks} \]

Half-life: 3-6 days, related to microsphere erosion and subsequent absorption of risperidone

Elimination phase is complete 7-8 weeks after last injection
Plasma Levels: 4-Week Delay in Impact of Dose Changes

Figure 6a. Blood levels from increasing a single dose from 25 mg to 50 mg at week 12 in an every 2 week schedule

Figure 6b. Blood levels from decreasing a single dose from 50 mg to 25 mg at week 12 in an every 2 week schedule

Plasma Levels: 4-Week Delay in Impact of Missed Dose

Figure 7. Blood levels following a single missed dose at week 12 in a schedule of 25 mg every 2 weeks

Figure 8. Blood levels following a dose given 1 week early at week 11 in a schedule of 25 mg every 2 weeks

Plasma Levels: 4-Week Delay in Impact of Missed Dose

Figure 9a. Blood levels following a dose given 1 week late at week 13 in a schedule of 25 mg every 2 weeks

Figure 9b. Blood levels following a dose given 3 weeks late at week 15 in a schedule of 25 mg every 2 weeks
Relapse Prevention With Risperidone Long-Acting Injectable (RLAI) vs. Oral Quetiapine

Gaebel W et al. Neuropsychopharmacology 2010;Epub ahead of print.
Awakeners Analysis:
Total PANSS ITT Population

30% Clinical Improvement
60% Clinical Improvement

* p < 0.05
** p < 0.01

Data on file, Janssen.
Paliperidone Palmitate

- Aqueous-based suspension of nanomolecular-sized crystals
- Due to its extremely low water solubility, paliperidone palmitate slowly dissolves at the injection site and is enzymatically hydrolyzed to paliperidone
- Kinetics are determined by particle size (might be a 3-month injection in the future!)
- Half-life: 25-49 days
- $T_{\text{max}}$: 13 days

Invega Sustenna Prescribing Information, Ortho-McNeil-Janssen.
Paliperidone Concentrations

*Initiation doses must be administered in the deltoid muscle.

Invega Sustenna Prescribing Information, Ortho-McNeil-Janssen.
Initial Sustenna Dosing

Initiation dosing: from oral

Day 1
- 234 mg Deltoid

1 week later
- 156 mg Deltoid
  ± 2 days
  Flexible dosing window‡

Maintenance doses q 4 wks

1 month later
- 37-234 mg Delt or Glut
  ± 1 week
  Flexible dosing window‡

1 month later
- 37-234 mg Delt or Glut
  ± 1 week
  Flexible dosing window‡

Initiation dosing from depot: When switching patients from long-acting injectable antipsychotics, give Sustenna in place of the next scheduled depot injection and then at monthly intervals. Dose is based on prior drug requirements. The 1-week initiation dosing regimen is not required.

Injection volumes are dose proportional: 234 mg - 1.5 mL, 156 mg - 1 mL, 117 mg - 0.75 mL, 78 mg - 0.5 mL, 39 mg - 0.25 mL

Invega Sustenna Prescribing Information, Ortho-McNeil-Janssen.
### Paliperidone Dose Equivalence

<table>
<thead>
<tr>
<th>Oral Risperidone Dose</th>
<th>IM Consta Dose Q2 Weeks</th>
<th>Oral Paliperidone ER Dose</th>
<th>IM Sustenna Dose Q4 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mg</td>
<td>25 mg</td>
<td>3 mg</td>
<td>39-78 mg</td>
</tr>
<tr>
<td>4 mg</td>
<td>37.5 mg</td>
<td>6 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>6 mg</td>
<td>50 mg</td>
<td>9 mg</td>
<td>156 mg</td>
</tr>
<tr>
<td>8 mg</td>
<td>?75 mg</td>
<td>12 mg</td>
<td>234 mg</td>
</tr>
</tbody>
</table>

Pivotal Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N</th>
<th>Duration</th>
<th>1° Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute trials in patients with acute exacerbation</td>
<td>Double-blind, placebo-controlled</td>
<td>197</td>
<td>9 wks</td>
<td>PANSS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>349</td>
<td>13 wks</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>513</td>
<td>13 wks</td>
<td>PANSS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>636</td>
<td>13 wks</td>
<td></td>
</tr>
<tr>
<td>Longer-term maintenance trial</td>
<td>Open-label transition and stabilization phase; double-blind, placebo-controlled</td>
<td>410</td>
<td>Transition/Stabilization: 33 wks Double-blind: up to 43 wks</td>
<td>Time to relapse</td>
</tr>
</tbody>
</table>

Maintenance study dose distribution:  
- **156 mg** - 69%  
- **78 mg** - 28%  
- **39 mg** - 2%

Invega Sustenna Prescribing Information, Ortho-McNeil-Janssen.
Efficacy of Paliperidone Palmitate

## Side Effect Profile by Maintenance Dose

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>39 mg</th>
<th>78 mg</th>
<th>156 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled data from 2 other 13-week, double-blind studies; incidence of EPS-related adverse events:</td>
<td>10%</td>
<td>12%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Parkinsonism:</td>
<td>7%</td>
<td>9%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>Akathisia:</td>
<td>4%</td>
<td>5%</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

Prolactin: increases are dose dependent and similar to those seen during oral risperidone or paliperidone treatment
Missed Second Dose Guidelines: by Time Since First Sustenna Injection

- < 4 weeks since the first injection (Day 1): give the second dose (156 mg) as soon as possible; the third dose should be given 5 weeks after the first injection regardless of the time of the second injection

- If 4-7 weeks have elapsed since the first injection: give a 156-mg dose in the deltoid as soon as possible and a second 156-mg dose in the other deltoid 1 week later

- If >7 weeks have elapsed since the first injection: reinitiate dosing with 234 mg IM (deltoid), then 156 mg IM (deltoid) 1 week later
Missed Dose Guidelines: Maintenance Dose by Time Since Last Sustenna Injection

• ≤ 6 weeks (e.g., ≤ 2 weeks late for monthly IM): give the previously stabilized dose

• > 6 weeks to 6 months: resume the same dose on which the patient was previously stabilized
  – If the patient was stabilized on a dose of 234 mg, then the first 2 injections should each be 156 mg, given as deltoid injections 1 week apart

• > 6 months: start over
Olanzapine Pamoate

- Practically insoluble salt
- Aqueous-based suspension is injected
- Mechanism for prolonged release
  - Due to its extremely low water solubility, olanzapine pamoate slowly dissolves at the injection site
  - Half-life: 30 days (18-41 days)
  - $T_{\text{max}}$: 3-4 days (2-7 days)
  - Injection volumes
    - 150 mg: 1.0 mL
    - 210 mg: 1.4 mL
    - 300 mg: 2.0 mL
    - 405 mg: 2.7 mL

Relprevv Prescribing Information, Eli Lilly, 2010.
### Olanzapine Dose Equivalence

<table>
<thead>
<tr>
<th>Daily Oral Olanzapine Dose</th>
<th>Relprevv Dose: First 8 weeks</th>
<th>Relprevv Dose: After 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>210 mg/2 wks OR 405 mg/4 wks</td>
<td>150 mg/2 wks OR 300 mg/4 wks</td>
</tr>
<tr>
<td>15 mg</td>
<td>300 mg/2 wks</td>
<td>210 mg/2 wks OR 405 mg/4 wks</td>
</tr>
<tr>
<td>20 mg</td>
<td>300 mg/2 wks</td>
<td>300 mg/2 wks</td>
</tr>
</tbody>
</table>

Oral supplementation was not used in clinical trials but may be necessary during the first few months. Relapse rates:
- **Lowest**: 10 mg/day oral → 300 mg/2 weeks (1.5%)
- **Highest**: 20 mg/day oral → 150 mg/2 weeks (18.8%)

Expected Olanzapine Levels Without Oral Coverage

Sedation Warning

- After each Relprevv injection, a healthcare professional must continuously observe the patient at the healthcare facility for at least 3 hours.

- Following the 3-hour observation period, healthcare professionals must confirm that the patient is alert, oriented, and absent of any signs and symptoms of post-injection delirium/sedation syndrome prior to being released.

- These events occurred in <0.1% of injections and in approximately 2% of patients who received injections for up to 46 months; these events were correlated with an unintentional rapid increase in serum olanzapine concentrations to supra-therapeutic ranges in some cases.

Relprevv Prescribing Information, Eli Lilly, 2010.
Finding: related to injection technique and either inadvertent intravascular injection or exposure of the injected product to a substantial volume of blood due to blood vessel injury during the injection with subsequent seepage of the medication into the vasculature.
Efficacy and Tolerability of Long-Acting Injectable Olanzapine

• Microsphere formulation with 2 week oral overlap

• Phase 1: Single-blind oral stabilization phase with aripiprazole monotherapy based on meeting all stability criteria for 4 consecutive weeks
  – Mean daily dose prior to randomization: 19.2 mg

**Stability criteria used to advance between phases:**

a. Outpatient status, PANSS total ≤ 80, with no score > 4 on core psychosis items

b. CGI-Severity ≤ 4 (moderately ill) and comparably low scores on suicidality scales
Aripiprazole Depot: Relapse Prevention Study, Later Phases

• Phase 2: Aripiprazole IM stabilization phase:
  – Transition to depot starting at 400 mg
  – 88.6% remained at the 400 mg dose
  – Among 710 who entered this phase, 576 (81%) were converted successfully to depot

• Phase 3. Randomization Phase: depot vs. placebo
  – Among 403 randomized patients, 96.3% stayed on 400 mg dose

• Conclusion: Aripiprazole depot superior to placebo on measures of relapse risk (HR 5.03, 95% CI 3.15-8.02, p<.0001)

• Double-blind side effects that occurred ≥ 5% and > 2x placebo: tremor (5.9%)
Summary

• For those who fail treatment due to non-adherence, depot medications show significant benefit

• Understanding kinetics is key to the effective use of depot medications

• Plasma drug levels may be useful during the maintenance phase to avoid levels outside the known therapeutic range

• In addition to conventional depot antipsychotics, there are several atypical depot antipsychotics available and several other depot formulations in development