

Unique Protocol ID: 13283

Secondary ID: H8Y-EW-HBCP

Brief Title: A Study to Test LY2140023 in Schizophrenia or Schizoaffective Disorder

Official Title: A Study Investigating the Potential Interaction Between LY2140023 and Antipsychotic Treatments in Subjects With Schizophrenia or Schizoaffective Disorder

Study Type: Interventional

Sponsor: Eli Lilly and Company

Collaborators: N/A

Brief Summary: The purpose of this study is to find out if LY2140023 causes any side effects when taken alone or in combination with other antipsychotic drugs. The amounts of LY2140023 and antipsychotic drugs that are in your body at different times will be measured to learn how the body breaks them down, uses them, and removes them.

After a screening visit, subjects will enter the clinic for the start of the observational period. Subjects will take their usual antipsychotic drugs throughout. After seven days in the clinic, dosing with LY2140023 will begin for a further seven days. Subjects will be in-patient in the clinic for 16 days in total. A final out-patient check-up will be done up to seven days later. After a screening visit, subjects will enter the clinic for the start of the observational period. Subjects will take their usual antipsychotic drugs throughout. After seven days in the clinic, dosing with LY2140023 will begin for a further seven days. Subjects will be in-patient in the clinic for 16 days in total. A final out-patient check-up will be done up to seven days later.

Overall Status: Completed

Study Start Date: November 2009

Study Completion Date: May 2010

Study Design:

Primary Purpose: Other

Study Phase: Phase 1

Interventional Model: Parallel Assignment

Number of Arms: 5

Masking: Open Label

Allocation: Non-Randomized

Control: Uncontrolled

Endpoint Classification: Safety Study

Enrollment: 120 Anticipated

Primary Outcome Measure:

Measure: Frequency of Adverse Events between groups

Timeframe: Over 7 days of treatment

Secondary Outcome Measure:

Measure: Pharmacokinetic comparison (Cmax and AUC) between groups

Timeframe: Over 7 days of treatment

Condition(s):

Schizophrenic Disorders

Schizoaffective Disorder

Arms	Assigned Interventions
Experimental: LY2140023	Drug: LY2140023 20 or 40 mg taken by mouth, twice daily, for 7 days
Experimental: Quetiapine + LY2140023	Drug: LY2140023 20 or 40 mg taken by mouth, twice daily, for 7 days Drug: Quetiapine Maximum of 800 mg per day taken by mouth, twice or three times daily for 7 days, at the subject's standard daily dose
Experimental: Aripiprazole + LY2140023	Drug: LY2140023 20 or 40 mg taken by mouth, twice daily, for 7 days Drug: Aripiprazole Maximum of 30 mg per day taken by mouth, once daily for 7 days, at the subject's standard daily dose

<p>Experimental: Olanzapine + LY2140023</p>	<p>Drug: LY2140023 20 or 40 mg taken by mouth, twice daily, for 7 days</p> <p>Drug: Olanzapine Maximum of 20 mg per day taken by mouth, once daily for 7 days, at the subject's standard daily dose</p>
<p>Experimental: Risperidone + LY2140023</p>	<p>Drug: LY2140023 20 or 40 mg taken by mouth, twice daily, for 7 days</p> <p>Drug: Risperidone Maximum of 16 mg per day taken by mouth, once or twice daily, at the subject's standard daily dose</p>

Eligibility Criteria:

Inclusion Criteria:

- Have a diagnosis of schizophrenia and/or schizoaffective disorder as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)
- Female subjects who test negative for pregnancy at screening and agree to use a reliable method of birth control during and for at least 3 months after the last LY2140023 dose.
- Female subjects who are postmenopausal. Postmenopausal is defined as no menses for at least 1 year, or a plasma follicular stimulating hormone value of > 40 IU/L, unless the subject is taking hormone replacement therapy.
- Male subjects with partners of child bearing potential must be willing to use barrier contraception in addition to having their partner use another method for the duration of the study and for three months after the last dose, and must be willing to abstain from sexual intercourse with pregnant or lactating women or use barrier methods for the duration of the study and for three months after the last dose.
- Subjects in group 1 must have no history or standard of care antipsychotic medication (SOC) use during the 7 days prior to entry into the observation period
- Subjects in group 2 must have been on a stable oral dose of SOC within the approved range in product labeling of one of the selected SOC's for at least 1 month prior to the observation period with no anticipation of changes to dose, regimen or treatment within the next 1 month
- Subjects in group 2 should not have had a change in antipsychotic medications for at least 12 weeks prior to the observation period
- Must be clinically stable according to the investigator
 - Should not have been hospitalized for psychiatric illness for at least 12 weeks prior to the observation period

- Must have a Clinical Global Impression-Severity Scale (CGI-S) score of < 4
- Must be willing and able to be hospitalized for the observation period and the duration of SOC and/or LY2140023 dosing period
- Be considered reliable, have a level of understanding sufficient to perform all tests and examinations required by the protocol, and be willing to perform all study procedures.
- Be able to understand the nature of the study and have given their own informed consent.
- Have venous access sufficient to allow blood sampling as per the protocol.
- Clinical laboratory test results at screening within an acceptable range for the population, or results with acceptable deviation that are judged to be not clinically significant by the investigator.
- Clinically acceptable sitting blood pressure and pulse rate, as determined by the investigator.

Exclusion Criteria:

- Are currently enrolled in, or discontinued within the 30 days prior to screening from, a clinical trial involving an investigational drug or concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study.
- Have previously completed or discontinued from this study or any other study investigating LY2140023 after having received at least 1 dose of LY2140023.
- Subjects for whom treatment with LY2140023, quetiapine, aripiprazole, olanzapine or risperidone as specified in the protocol, is relatively or absolutely clinically contraindicated.
- Subjects who have received treatment with clozapine at doses greater than 200 mg daily within 12 months prior to screening, or who have received any clozapine at all during the month before screening.
- Subjects who are taking any antipsychotic medication other than those included in this study.
- Subjects who are taking any of the following: oral antifungals (ie. ketoconazole), oral corticosteroids (ie. prednisone), antiarrhythmics (ie. digoxin, sotalol), protease inhibitors (ie. ritonavir), immunosuppressants (ie. cyclosporine, methotrexate, Gold compounds), tumor necrosis factor inhibitors (ie. enbrel), lithium, bupropion, pseudoephedrine, reserpine, or varenicline. The use of anticonvulsant medications, other than for the documented treatment of mood-stabilization, is prohibited.
- Subjects receiving treatment with depot antipsychotic medication within 12 weeks, prior to screening.
- Subjects who have answered 'yes' to either Question 4 (Active Suicidal Ideation with Some Intent to Act, Without Specific Plan) or Question 5 (Active Suicidal Ideation with Specific Plan and Intent) on the "Suicidal Ideation" portion of the Columbia suicide severity rating scale (C-SSRS), or answer "yes" to any of the suicide-related behaviors (actual attempt, interrupted attempt, aborted attempt, preparatory act or behavior) on the "Suicidal Behavior" portion of the C-SSRS; and the ideation or behavior occurred within the past month.
- DSM-IV-TR diagnosis of substance dependence or substance abuse (except nicotine and caffeine) within the 6 months prior to screening.

- Diagnosis of substance-induced psychosis by DSM-IV-TR criteria within 7 days of screening (or at any time during the study).
- Female subjects who are pregnant, nursing, or who intend to become pregnant within 3 months of completing the study.
- Have donated blood of more than 500 mL within the last month before screening.
- Have a history of one or more seizures, including those who experienced a single simple febrile seizure between ages 6 months and 5 years (a single simple febrile seizure is defined as lacking focality and lasting less than 15 minutes, not associated with a central nervous system (CNS) infection or severe metabolic disturbance), or subjects are excluded if they have met one or more of the following criteria:
 - Have a first degree relative (that is, biological father, mother, brother, sister or child) with history of idiopathic epilepsy
 - Within 1 year of screening subjects have a history of CNS infection, uncontrolled migraine, transient ischemic attack (TIA), or head trauma with loss of consciousness or a post-concussive syndrome.
 - A lifetime history of any of the following:
 - head trauma, stroke, or CNS infection with persistent neurological deficit(focal or diffuse)
 - brain surgery
 - an EEG with paroxysmal (epileptiform) activity, for example, one that demonstrates 3 or more focal sharp or spike waves, any sharp and slow wave complex, or any epileptiform discharge that is rhythmic, sustained, or generalized, or as locally defined
 - brain structural lesion, including developmental abnormalities, as determined by examination or imaging studies.
- Have a screening electroencephalogram (EEG) with paroxysmal (epileptiform) activity, for example, one that demonstrates 3 or more focal sharp or spike waves, any sharp and slow wave complex, or any epileptiform discharge that is rhythmic, sustained, or generalized, or as locally defined.
- Subjects who have had electroconvulsive therapy (ECT) within 3 months of screening or who are expected to have ECT at any time during the study.
- A diagnosis of Parkinson's disease, dementia-related psychosis, or related disorders.
- Subject with untreated hyperthyroidism or hypothyroidism needing a thyroid hormone supplement who have not been on a stable dose of medication for at least 2 months prior to screening.
- Have leukopenia or history of leukopenia without a clear and resolved etiology, or known history of agranulocytosis (absolute neutrophil count <500/mm³, or <0.5 GI/L, or <0.5 10³/uL) during the subject's lifetime.
- Show evidence of human immunodeficiency virus (HIV) and/or positive human HIV antibodies.
- Evidence of hepatitis C and/or positive hepatitis C antibody
- Evidence of hepatitis B and/or positive hepatitis B surface antigen.
- Subjects with alanine aminotransferase (ALT/SGPT) or aspartate aminotransferase (AST/SGOT) values >2 times the upper limit of normal (ULN) of the performing laboratory, or total bilirubin values >1.5 times the ULN of the performing laboratory at screening.

- Have acute, serious or unstable medical conditions, including (but not limited to) inadequately controlled diabetes (HgbA1c >8%), severe hypertriglyceridemia (fasting triglycerides >500 mg/dL), hepatic insufficiency (specifically any degree of jaundice), recent cerebrovascular accidents, seizure disorders, serious acute systemic infection or immunology disease, unstable cardiovascular disorders (including ischemic heart disease), renal, gastroenterologic, respiratory, endocrinologic, neurologic, or hematologic diseases (specifically current absolute neutrophil count <1,500/mm³).
- Prolactin level of >200 ng/mL (200 ug/L, or 4228 mIU/L) at screening with the exception of subjects treated with risperidone. Subjects treated with risperidone are excluded if the prolactin level is >300 ng/mL (300 ug/L, or 6342 mIU/L) at screening).
- Subjects with a corrected QT interval (Bazett's; QTcB) >450 msec (male) or >470 msec (female) at screening.
- Show evidence of active renal disease (for example, diabetic renal disease, polycystic kidney disease) or creatinine clearance (CrCl) less than 80 mL/min (as calculated by Cockcroft-Gault equation

Minimum Age: 18

Maximum Age: 55

Gender: both

Contact for Public Queries: Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST)

Contact for Scientific Queries: Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST)

Locations:

Lilly Clinical Trial Site
Willingboro, New Jersey, United States
Completed

Lilly Clinical Trial Site
Garden Grove, California, United States
Completed

Lilly Clinical Trial Site
Austin, Texas, United States
Completed

Lilly Clinical Trial Site
Glendale, California, United States
Completed