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Requires Data Access? Yes

Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.

How did you learn about the YODA Project?: Colleague

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2019/04/stefan_leucht.pdf
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Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT00488319 - R076477PSZ3002 - A 2-Year, Open-Label, Single-Arm Safety Study of Flexibly Dosed Paliperidone Extended Release (1.5-12 mg/day) in the Treatment of Adolescents (12 to 17 Years of Age) With Schizophrenia
2. NCT01009047 - R076477PSZ3003 - A Randomized, Multicenter, Double-Blind, Active-Controlled, Flexible-Dose, Parallel-Group Study of the Efficacy and Safety of Prolonged Release Paliperidone for the Treatment of Symptoms of Schizophrenia in Adolescent Subjects, 12 to 17 Years of Age
3. NCT00645099 - R076477SCH3020 - A Prospective Randomized Open-label 6-Month Head-To-Head Trial to Compare Metabolic Effects of Paliperidone ER and Olanzapine in Subjects With Schizophrenia
4. NCT00518323 - R076477PSZ3001 - A Randomized, Multicenter, Double-Blind, Weight-Based, Fixed-Dose, Parallel-Group, Placebo-Controlled Study of the Efficacy and Safety of Extended Release Paliperidone for the Treatment of Schizophrenia in Adolescent Subjects, 12 to 17 Years of Age
5. NCT01606228 - R076477SCH3033 - An Open-Label Prospective Trial to Explore the Tolerability, Safety and Efficacy of Flexibly-Dosed Paliperidone ER among Treatment-Naive and Newly Diagnosed Patients with Schizophrenia
6. NCT00334126 - R076477SCH3015 - A Randomized, Double-blind, Placebo-controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Paliperidone ER Compared to Quetiapine in Subjects With an Acute Exacerbation of Schizophrenia
7. NCT00086320 - R076477-SCH-301 - A Randomized, Double-blind, Placebo-controlled, Parallel-group Study With an Open-label Extension Evaluating Paliperidone Extended Release Tablets in the Prevention of Recurrence in Subjects With Schizophrenia
8. NCT00589914 - R092670PSY3006 - A Randomized, Double-Blind, Parallel-Group, Comparative Study of Flexible Doses of Paliperidone Palmitate and Flexible Doses of Risperidone Long-Acting Intramuscular Injection in Subjects With Schizophrenia
9. NCT00604279 - R092670PSY3008 - A Randomized, Open-Label, Parallel Group Comparative Study of Paliperidone Palmitate (50, 100, 150 mg eq) and Risperidone LAI (25, 37.5, or 50 mg) in Subjects with Schizophrenia
10. NCT00590577 - R092670PSY3007 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (25 mg eq., 100 mg eq., and 150 mg eq.) of Paliperidone Palmitate in Subjects With Schizophrenia
11. NCT00111189 - R092670PSY3001 - A Randomized Double-blind Placebo-controlled Parallel Group Study Evaluating Paliperidone Palmitate in the Prevention of Recurrence in Patients With Schizophrenia, Placebo Consists of 20% Intralipid (200 mg/mL) Injectable Emulsion
12. NCT00210717 - R092670PSY3002 - A Randomized, Double-Blind, Parallel Group, Comparative

Study of Flexibly Dosed Paliperidone Palmitate (25, 50, 75, or 100 mg eq.) Administered Every 4 Weeks and Flexibly Dosed RISPERDAL CONSTA (25, 37.5, or 50 mg) Administered Every 2 Weeks in Subjects With Schizophrenia

13. NCT00119756 - R092670PSY3005 - A Randomized, Crossover Study to Evaluate the Overall Safety and Tolerability of Paliperidone Palmitate Injected in the Deltoid or Gluteus Muscle in Patients With Schizophrenia
14. NCT00210548 - R092670PSY3003 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (50 mg eq., 100 mg eq., and 150 mg eq.) of Paliperidone Palmitate in Subjects With Schizophrenia
15. NCT00101634 - R092670PSY3004 - A Randomized, Double-blind, Placebo-controlled, Parallel-group, Dose-response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (25 mg eq, 50 mg eq, and 100 mg eq) of Paliperidone Palmitate in Patients With Schizophrenia
16. NCT00391222 - RISBMN3001 - A Randomized, Double Blind, Placebo and Active Controlled Parallel Group Study to Evaluate the Efficacy and Safety of Risperidone Long-acting Injectable (LAI) for the Prevention of Mood Episodes in the Treatment of Subjects With Bipolar I Disorder
17. NCT00034749 - RIS-USA-231 - The Efficacy and Safety of Risperidone in Adolescents With Schizophrenia: a Comparison of Two Dose Ranges of Risperidone
18. NCT00076115 - RIS-BIM-301 - Research on the Effectiveness of Risperidone in Bipolar Disorder in Adolescents and Children (REACH): A Double-Blind, Randomized, Placebo-Controlled Study of the Efficacy and Safety of Risperidone for the Treatment of Acute Mania in Bipolar I Disorder
19. NCT00132678 - RISBIM3003 - A Randomized, Double-blind, Placebo-controlled Study to Explore the Efficacy and Safety of Risperidone Long-acting Intramuscular Injectable in the Prevention of Mood Episodes in Bipolar 1 Disorder, With Open-label Extension
20. NCT00094926 - RIS-BIP-302 - A Prospective, Randomized, Double-blind, Placebo-controlled Study of the Effectiveness and Safety of RISPERDAL CONSTA Augmentation in Adult Patients With Frequently-relapsing Bipolar Disorder
21. NCT00397033 - R076477SCA3001 - A Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Two Dosages of Paliperidone ER in the Treatment of Patients With Schizoaffective Disorder
22. NCT00412373 - R076477SCA3002 - A Randomized, Double-blind, Placebo-controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Flexible-dose Paliperidone ER in the Treatment of Patients With Schizoaffective Disorder
23. NCT00236444 - CR002020 (RIS-INT-79) - Risperidone in the Prevention of Relapse: a Randomized, Double-blind, Placebo-controlled Trial in Children and Adolescents With Conduct and Other Disruptive Behavior Disorders
24. NCT00236470 - CR002149 (RIS-INT-84) - Risperidone in the Treatment of Children and Adolescents With Conduct and Other Disruptive Behavior Disorders - an Open Label Follow-up Trial of CR002020
25. NCT00250354 - CR006007 (RIS-CAN-19) - The Safety And Efficacy Of Risperidone Versus Placebo In Conduct Disorder In Mild, Moderate And Borderline Mentally Retarded Children Aged 5 To 12 Years
26. NCT00266552 - CR006019 (RIS-USA-93) - The Safety And Efficacy Of Risperidone Versus Placebo In Conduct Disorder and Other Disruptive Behavior Disorders In Mild, Moderate And Borderline Mentally Retarded Children Aged 5 To 12 Years
27. NCT00249132 - RIS-INT-3 - A Canadian multicenter placebo-controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenic patients
28. NCT00216476 - RISSCH3001 - CONSTATRE: Risperdal(R) Consta(R) Trial of Relapse Prevention and Effectiveness
29. NCT00216580 - RIS-PSY-301 - An Open-label Trial of Risperidone Long-acting Injectable in the Treatment of Subjects With Recent Onset Psychosis
30. NCT00253162 - RIS-INT-69 - The Efficacy And Safety Of Flexible Dose Ranges Of Risperidone Versus Placebo Or Haloperidol In The Treatment Of Manic Episodes Associated With Bipolar I Disorder
31. NCT00378092 - CR011992, RISSCH3024 - A Prospective Study of the Clinical Outcome Following Treatment Discontinuation After Remission in First-Episode Schizophrenia
32. NCT00299715 - R076477-BIM-3001 - A Randomized, Double-Blind, Placebo-Controlled,

Parallel-Group, Dose-Response, Multicenter Study to Evaluate the Efficacy and Safety of Three Fixed Doses of Extended-Release Paliperidone in the Treatment of Subjects With Acute Manic and Mixed Episodes Associated With Bipolar I Disorder

33. NCT00309699 - R076477-BIM-3002 - A Randomized, Double-Blind, Active- and Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Flexibly-Dosed, Extended-Release Paliperidone Compared With Flexibly-Dosed Quetiapine and Placebo in the Treatment of Acute Manic and Mixed Episodes Associated With Bipolar I Disorder
34. NCT00309686 - R076477-BIM-3003 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Flexibly-Dosed Extended-Release Paliperidone as Adjunctive Therapy to Mood Stabilizers in the Treatment of Acute Manic and Mixed Episodes Associated With Bipolar I Disorder
35. NCT00752427 - R076477-SCH-702 - 24 week extension of NCT00085748: A Randomized, 6-Week Double-Blind, Placebo-Controlled Study With an Optional 24-Week Open-Label Extension to Evaluate the Safety and Tolerability of Flexible Doses of Paliperidone Extended Release in the Treatment of Geriatric Patients With Schizophrenia
36. NCT00077714 - R076477-SCH-304 - A Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Dose-response Study to Evaluate the Efficacy and Safety of 2 Fixed Dosages of Paliperidone Extended Release Tablets and Olanzapine, With Open-label Extension, in the Treatment of Patients With Schizophrenia
37. NCT00083668 - R076477-SCH-305 - A Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Dose-response Study to Evaluate the Efficacy and Safety of 3 Fixed Dosages of Paliperidone Extended Release (ER) Tablets and Olanzapine, With Open-label Extension, in the Treatment of Patients With Schizophrenia
38. NCT00074477 - R092670-SCH-201 - A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of 50 and 100 Mg-eq of Paliperidone Palmitate in Patients With Schizophrenia
39. NCT00078039 - R076477-SCH-303 - Trial Evaluating Three Fixed Dosages of Paliperidone Extended-Release (ER) Tablets and Olanzapine in the Treatment of Patients With Schizophrenia
40. NCT00085748 - R076477-SCH-302 - A Randomized, 6-Week Double-Blind, Placebo-Controlled Study With an Optional 24-Week Open-Label Extension to Evaluate the Safety and Tolerability of Flexible Doses of Paliperidone Extended Release in the Treatment of Geriatric Patients With Schizophrenia
41. NCT00249158 - RIS-AUS-5/CR006010 - Risperidone in the Treatment of Behavioural and Psychological Signs and Symptoms in Dementia (BPSSD): a Multicentre, Double-blind, Placebo-controlled Parallel-group Trial
42. - RIS-BEL-14 - Risperidone in the treatment of behavioural disturbances in patients with Alzheimer's dementia: a double-blind placebo-controlled trial
43. NCT00261508 - RIS-CAN-23/CR006106 - Efficacy And Safety Of Risperidone In The Treatment Of Children With Autistic Disorder And Other Pervasive Developmental Disorders: A Canadian, Multicenter, Double-Blind, Placebo-Controlled Study
44. NCT00249236 - RIS-IND-2/CR006064 - The Efficacy And Safety Of Flexible Dosage Ranges Of Risperidone Versus Placebo In The Treatment Of Manic Or Mixed Episodes Associated With Bipolar I Disorder
45. NCT00249145 - RIS-INT-24/CR006046 - Risperidone in the Treatment of Behavioral Disturbances in Demented Patients: an International, Multicenter, Placebo-controlled, Double-blind, Parallel-group Trial Using Haloperidol as Internal Reference
46. NCT00250367 - RIS-INT-46/CR006058 - The Safety And Efficacy Of Risperdal (Risperidone) Versus Placebo As Add-On Therapy To Mood Stabilizers In The Treatment Of The Manic Phase Of Bipolar Disorder
47. - RIS-INT-83 - Efficacy and safety of a flexible dose of risperidone versus placebo in the treatment of psychosis of Alzheimer's disease. A double-blind, placebo-controlled, parallel-group study.
48. NCT00088075 - RIS-SCH-302/CR003370 - A Randomized, Double-Blind, Placebo-Controlled Clinical Study of the Efficacy and Safety of Risperidone for the Treatment of Schizophrenia in Adolescents
49. - RIS-USA-1 (RIS-USA-9001) - Risperidone versus haloperidol versus placebo in the treatment

of schizophrenia
50. NCT00253149 - RIS-USA-102/CR006040 - The Safety And Efficacy Of Risperdal (Risperidone) Versus Placebo Versus Haloperidol As Add-On Therapy To Mood Stabilizers In The Treatment Of The Manic Phase Of Bipolar Disorder
51. NCT00253136 - RIS-USA-121/CR006055 - Risperidone Depot (Microspheres) vs. Placebo in the Treatment of Subjects With Schizophrenia
52. - RIS-USA-150 - A double-blind, placebo-controlled study of risperidone in children and adolescents with autistic disorder
53. NCT00034762 - RIS-USA-232/CR002764 - Efficacy And Safety Of A Flexible Dose Of Risperidone Versus Placebo In The Treatment Of Psychosis Of Alzheimer's Disease
54. NCT00257075 - RIS-USA-239/CR006052 - The Efficacy And Safety Of Flexible Dosage Ranges Of Risperidone Versus Placebo In The Treatment Of Manic Episodes Associated With Bipolar I Disorder
55. - RIS-USA-240 - The efficacy and safety of flexible dose ranges of risperidone vs. Placebo or divalproex sodium in the treatment of manic or mixed episodes associated with bipolar 1 disorder
56. NCT00253123 - RIS-USA-63/CR006022 - A Randomized, Double-Blind, Placebo-Controlled Study of Risperidone for Treatment of Behavioral Disturbances in Subjects With Dementia
57. - RIS-USA-72 - The safety and efficacy of risperidone 8 mg qd and 4 mg qd compared to placebo in the treatment of schizophrenia
58. NCT01529515 - R092670PSY3012 - A Randomized, Multicenter, Double-Blind, Relapse Prevention Study of Paliperidone Palmitate 3 Month Formulation for the Treatment of Subjects With Schizophrenia
59. NCT01193153 - R092670SCA3004 - A Randomized, Double-Blind, Placebo-Controlled, Parellel-Group Study of Paliperidone Palmitate Evaluating Time to Relapse in Subjects With Schizoaffective Disorder
60. NCT01662310 - R076477-SCH-3041 - Paliperidone Extended Release Tablets for the Prevention of Relapse in Subjects With Schizophrenia: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study
61. NCT00490971 - R076477BIM3004 - A Randomized, Double-Blind, Active- and Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Efficacy and Safety of Extended-Release Paliperidone as Maintenance Treatment After an Acute Manic or Mixed Episode Associated With Bipolar I Disorder
62. NCT00524043 - R076477SCH4012 - A Randomized, Double-Blind, Placebo- and Active-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of a Fixed Dosage of 1.5 mg/Day of Paliperidone Extended Release (ER) in the Treatment of Subjects With Schizophrenia
63. NCT00105326 - R076477-SCH-1010/CR002281 - A Double-blind, Placebo-controlled, Randomized Study Evaluating the Effect of Paliperidone ER Compared With Placebo on Sleep Architecture in Subjects With Schizophrenia
64. - RIS-USA-70 (EXTENSION OF RIS-USA-63) CR003361, RIS-USA-T216 - An open-label, long-term study of risperidone for the treatment of behavioral disturbances in patients with dementia
65. NCT00246246 - RIS-BIP-301 - A Randomized, Open-label Trial of RISPERDAL(R) CONSTA(TM) Versus Oral Antipsychotic Care in Subjects With Bipolar Disorder
66. NCT00044681 - RIS-INT-93 - A Study to Evaluate the Efficacy, Safety and Maintenance Effect of Risperidone Augmentation of SSRI Monotherapy in Young and Older Adult Patients With Unipolar Treatment-Resistant Depression
67. NCT00249223 - RIS-INT-61 - Risperidone Depot (Microspheres) vs. Risperidone Tablets - a Non-inferiority, Efficacy Trial in Subjects With Schizophrenia
68. NCT01157351 - R092670SCH3006 - A Fifteen-month, Prospective, Randomized, Active-controlled, Open-label, Flexible Dose Study of Paliperidone Palmitate Compared With Oral Antipsychotic Treatment in Delaying Time to Treatment Failure in Adults With Schizophrenia Who Have Been Incarcerated
69. NCT01081769 - R092670SCH3005 - A 24-month, Prospective, Randomized, Active-Controlled, Open-Label, Rater-Blinded, Multicenter, International Study of the Prevention of Relapse Comparing Long-Acting Injectable Paliperidone Palmitate to Treatment as Usual With Oral Antipsychotic Monotherapy in Adults With Schizophrenia

70. NCT01281527 - R092670SCH3010 - A 6-month, Open Label, Prospective, Multicenter, International, Exploratory Study of a Transition to Flexibly Dosed Paliperidone Palmitate in Patients With Schizophrenia Previously Unsuccessfully Treated With Oral or Long-acting Injectable Antipsychotics
71. NCT01051531 - R092670SCH3009 - Safety, Tolerability, and Treatment Response of Paliperidone Palmitate in Subjects With Schizophrenia When Switching From Oral Antipsychotics
72. NCT01527305 - R092670SCH4009 - An Open-Label, Prospective, Non-Comparative Study to Evaluate the Efficacy and Safety of Paliperidone Palmitate in Subjects With Acute Schizophrenia
73. NCT01299389 - PALM-JPN-4 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Fixed-Dose, Multicenter Study of JNS010 (Paliperidone Palmitate) in Patients With Schizophrenia
74. NCT01258920 - PALM-JPN-5 - A Long-Term, Open-Label Study of Flexibly Dosed Paliperidone Palmitate Long-Acting Intramuscular Injection in Japanese Patients With Schizophrenia
75. NCT00216671 - RISSCH4045 - Early Versus Late Initiation of Treatment With Risperdal Consta in Subjects With Schizophrenia After an Acute Episode
76. NCT00369239 - RISSCH4043 - Is Premorbid Functioning a Predictor of Outcome in Patients With Early Onset Psychosis Treated With Risperdal Consta?
77. NCT00216632 - RISSCH4026 - Treatment Success in Patients Requiring Treatment Change From Olanzapine to Risperidone Long Acting Injectable (TRESOR)
78. NCT00236379 - RIS-USA-275 - A Six-month, Double-blind, Randomized, International, Multicenter Trial to Evaluate the Glucoregulatory Effects of Risperidone and Olanzapine in Subjects With Schizophrenia or Schizoaffective Disorder
79. NCT00576732 - RISAUT4002 - Risperidone in the Treatment of Children and Adolescents With Autistic Disorder: A Double-Blind, Placebo-Controlled Study of Efficacy and Safety, Followed by an Open-Label Extension Study of Safety
80. NCT01050582 - RISNAP4022 - Evaluation of Growth, Sexual Maturation, and Prolactin-Related Adverse Events in the Pediatric Population Exposed to Atypical Antipsychotic Drugs
81. NCT00086112 - RIS-ANX-301 - A Double-blind, Randomized, Prospective Study to Evaluate Adjunctive Risperidone Versus Adjunctive Placebo in Generalized Anxiety Disorder Sub-optimally Responsive to Standard Psychotropic Therapy
82. NCT00216528 - RIS-KOR-66 - A Prospective, Open-Label Study to Evaluate Symptomatic Remission in Schizophrenia With Long Acting Risperidone Microspheres (Risperdal Consta)
83. NCT00269919 - RIS-KOR-64 - Effect on Efficacy, Safety and Quality of Life by Long-Term Treatment of Long-Acting Risperidone Microspheres in Patients With Schizophrenia
84. NCT00992407 - RISSCH4178 - A Randomized, Open-label, Active-controlled Study to Evaluate Social Functioning of Long Acting Injectable Risperidone and Oral Risperidone in the Treatment of Subjects With Schizophrenia or Schizoaffective Disorder
85. NCT00236353 - RIS-USA-305 - An Open-label Study of the Efficacy and Safety of RISPERDAL Long-acting Microspheres (RISPERDAL CONSTA) Administered Once Monthly in Adults With Schizophrenia or Schizoaffective Disorder
86. NCT00495118 - RIS-INT-80 - Risperidone Depot (Microspheres) in the Treatment of Subjects With Schizophrenia or Schizoaffective Disorder - an Open-label Follow-up Trial of RIS-INT-62 and RIS-INT-85
87. NCT01855074 - RISSCH4186 - Evaluation of Efficacy and Safety of Risperidone in Long-acting Microspheres in Patients With Schizophrenia, Schizophreniform or Schizoaffective Disorders Diagnosed According to the DSM-IV Criteria, After Switching Treatment With Any Antipsychotic Therapy With Long-acting Microspheres of Risperidone
88. NCT00236457 - RIS-INT-62 - Randomized, Multi-center, Open Label Trial Comparing Risperidone Depot (Microspheres) and Olanzapine Tablets in Patients With Schizophrenia or Schizoaffective Disorder
89. NCT00236587 - RIS-USA-265 - An Open Label, Long Term Trial of Risperidone Long Acting Microspheres in the Treatment of Patients Diagnosed With Schizophrenia
90. NCT00297388 - RIS-SCH-401 - A 52-wk Prospective, Randomized, Double-blind, Multicenter Study of Relapse Following Transition From Oral Antipsychotic Medication to 2 Different Doses (25 or 50 mg Every 2 Wks) of Risperidone Long-acting Microspheres (RISPERDAL CONSTA) in Adults With Schizophrenia or Schizoaffective Disorder

91. NCT00821600 - RIS-SCH-1012 - Single-Dose, Open-Label Pilot Study to Explore the Pharmacokinetics, Safety and Tolerability of a Gluteal Intramuscular Injection of a 4-Week Long-Acting Injectable Formulation of Risperidone in Patients With Chronic Stable Schizophrenia
92. NCT00526877 - RISSCH4119 (RISC-TWN-MA10) - Evaluation of Efficacy and Safety of Long-acting Risperidone Microspheres in Patients With Schizophrenia or Schizoaffective Disorders, Who is Receiving Psychiatric Home-care Treatment, When Switching From Typical Depot or Oral Antipsychotics to Long-acting Risperidone Microspheres
93. NCT00061802 - RIS-SCP-402 - A Randomized, Double Blind Study to Evaluate the Efficacy and Safety of Two Atypical Antipsychotics vs. Placebo in Patients With an Acute Exacerbation of Either Schizophrenia or Schizoaffective Disorder
94. NCT01624675 - RIS-AUT-JPN-01 - A Double-blind, Placebo-controlled Study, Followed by an Open-label Extension Study Evaluating the Efficacy and Safety of Risperidone (R064766) in Children and Adolescents With Irritability Associated With Autistic Disorder
95. NCT00034775 - RIS-USA-259 - Open-Label Trial Exploring A Switching Regimen From Oral Neuroleptics, Other Than Risperidone, To Risperidone Depot Microspheres
96. NCT00460512 - R076477SCH3017 - An Open-label Prospective Trial to Explore the Tolerability, Safety and Efficacy of Flexibly Dosed Paliperidone ER in Subjects With Schizophrenia
97. NCT00566631 - R076477SCH3018 - Tolerability, Safety and Treatment Response of Flexible Doses of Paliperidone ER in Acutely Exacerbated Subjects With Schizophrenia
98. NCT01515423 - R092670PSY3011 - A Randomized, Multicenter, Double-Blind, Non-inferiority Study of Paliperidone Palmitate 3 Month and 1 Month Formulations for the Treatment of Subjects With Schizophrenia
99. NCT02713282 - R092670SCH3015 - A 52-Week, Open-Label, Prospective, Multicenter, International Study of a Transition to the Paliperidone Palmitate 3-Month Formulation In Patients With Schizophrenia Previously Stabilized on the Paliperidone Palmitate 1-Month Formulation
100. NCT00095134 - RIS-DEP-401 - A Double-Blind Study Comparing Adjunctive Risperidone Versus Placebo in Major Depressive Disorder That Is not Responding to Standard Therapy

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Temporal trajectories of side-effects associated with antipsychotic treatment ? An individual participant data meta-analysis

Narrative Summary:

Antipsychotics are the mainstem for the treatment of schizophrenia and other mental disorder. While use of antipsychotics is essential for favorable outcomes in terms of acute efficacy and relapse prevention, it can cause various unpleasant side effects (1). These side effects are associated with a lower quality of life and poorer adherence in patients (2). It is known that patients acquire tolerance to some side effects in clinical practice whereas others may get more severe over time. However, the temporal trajectories of side effects are yet unclear. Therefore, we will investigate temporal trajectories (e.g., onset, duration) of side effects associated with antipsychotic treatment.

Scientific Abstract:

Background: Antipsychotics are the mainstem for treating schizophrenia and other mental disorders.

While use of antipsychotic treatment is essential for favorable outcomes in terms of acute efficacy and relapse prevention, the use of antipsychotics can cause various unpleasant side effects such as sedation, extrapyramidal symptoms, hyperprolactinemia, metabolic and cardiovascular disturbances, and anticholinergic side effects (1). These side effects are associated with a lower quality of life and poorer adherence in patients (2). It is known that patients acquire tolerance to some side effects in clinical practice whereas other side effects may get more severe over time. However, it is unclear when side effects occur and disappear.
Objective: We aim to systematically assess the occurrence, onset, duration and severity of side effects associated with antipsychotic treatment.
Study Design: This study is an Individual-Patient-Data (IPD) meta-analysis of clinical trials to evaluate the occurrence, onset, duration and severity of side effects associated with antipsychotic treatment.
Participants: Participants in clinical trials of antipsychotic drug monotherapy irrespective of diagnosis, age, gender, and ethnicity.
Main Outcome Measures: The occurrence, onset, duration, and severity of side effects associated with antipsychotic treatment
Statistical Analysis: The median time to onset and the duration of side effects will be calculated from synthesized data by IPD meta analysis.

Brief Project Background and Statement of Project Significance:

Antipsychotics are the mainstem for the treatment of schizophrenia and used for the treatment of other psychiatric diseases. While the use of antipsychotic therapy is essential for favorable outcomes in terms of acute efficacy and relapse prevention, the use of antipsychotics can cause various unpleasant side effects such as sedation, extrapyramidal symptoms, hyperprolactinemia, metabolic and cardiovascular disturbances, and anticholinergic side effects (1). The impacts of side effects vary widely, ranging from very unpleasant in daily life (e.g., sedation, akathisia, weight gain, and constipation) to life-threatening (e.g., neuroleptic malignant syndrome, pneumonia, thromboembolism, and sudden cardiac death). Given these side effects are associated with a lower quality of life and poorer adherence in patients (2), proper management of side effects is important for a long-term treatment. However, the timeline of side effects has not been systematically studied. Knowing for example when side effects occur and disappear not only allows clinicians to optimize treatment with antipsychotics, but also helps patients monitor and manage their side effects. Therefore, this study aims to systematically assess the occurrence, onset, duration, and severity of side effects associated with antipsychotic treatment.

Specific Aims of the Project:

The purpose of this project is to systematically assess temporal trajectories (the occurrence, onset, duration, and severity) of side effects associated with antipsychotic treatment and factors that could influence them.
Primary objective:
Evaluate temporal trajectories of antipsychotic-associated side-effects, e.g., time of onset, duration, temporal changes in severity, and time of disappearance.
Secondly objectives:
Evaluate factors (e.g., type of antipsychotic, dosage) that could influence temporal trajectories of antipsychotic-associated side-effects.

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

We will consider prospective trials investigating the antipsychotic treatment in monotherapy without further restrictions, such as in terms of randomization, blinding, or follow-up duration. Any antipsychotic drug (ATC codes of N05., except lithium N05AN01) or placebo will be eligible. All participants in eligible studies will be included, irrespective of underlying diagnosis (e.g., schizophrenia, schizoaffective disorder, bipolar disorder, and children with disruptive behavior

disorder), stage and severity of illness (e.g., acute, chronic), age (e.g., children, adolescent, and adults), gender, ethnicity, and comorbidities.

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

We will investigate temporal trajectories of antipsychotic-associated side-effects (e.g., time of onset, duration, changes in their severity, and time of disappearance).
We will consider 1) adverse events, such as extrapyramidal symptoms, akathisia, sedation, weight gain, prolactin elevation, QTc prolongation, and anticholinergic side-effects (e.g., constipation, blurred vision) We will use the Medical Dictionary for Regulatory Activities Terminology (MedDRA)(3) for the classification of adverse events. We will also consider 2) rating scale measures (e.g., Drug Induced Extra Pyramidal Symptoms Scale, Simpson-Angus Extrapyramidal Rating Scale, UKU side effect rating scale, Visual Analog Scale, Barnes Akathisia Rating Scale), and 3) biological measures (e.g., body weight, corrected QT interval on ECG, blood pressure, prolactin, blood glucose)

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

The use of antipsychotics will be the independent variable.
The independent variable allows us to investigate the relationship between antipsychotic use and the onset, duration, and severity of the side effects of antipsychotics.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

We will consider factors with a potential influence on the temporal trajectories of antipsychotic-associated side-effects, such as specific antipsychotics, dosage of antipsychotics, administration route of antipsychotics, age, gender, ethnicity, diagnosis, life-time antipsychotic exposure (when not available, duration of illness will be used as a proxy in participants with schizophrenia), comorbid disorders, family history, smoking, baseline BMI, measures of psychopathology, and concomitant medications, etc.

Statistical Analysis Plan:

First, we will conduct descriptive analysis on time to onset and duration of side effects, and then with statistical models that take temporal trajectories into account, such as the Kaplan-Meier method for binary adverse event data and Mixed-Models-of-Repeated-Measurements (MMRM) for rating-scale outcomes and biological measures. The effect size measures will be the time to onset and the time to resolution for binary adverse events and the change from baseline for rating-scale-outcomes or biological measures.
We consider occurrence and duration of somatic side effects of antipsychotics rather independent of the underlying psychiatric disease (e.g., schizophrenia or bipolar disorder) and therefore, we include a priori studies in different disorders. However, we expect variability in the effects due to differences in participant, intervention, and study characteristics. Therefore, we will explore sources of heterogeneity by subgroup and meta-regression analyses on potentially important effect modifiers such as age, sex, diagnosis (to investigate our assumption above), previous antipsychotic exposure, type, application and dose of antipsychotic, trial duration, RCT (Randomized control trial) and not RCT, ? (see list of ?Other Variables of Interest? above).
Variables which emerge as having a substantial effect on occurrence and duration of side effects will be included in the statistical model by introducing interactions.
We will handle missing outcome and covariate data following Little et al.(4) and impute it, when scientifically sound, by multiple imputations.
Effect size measures and covariates of different studies will be synthesized with meta-analysis.
I-squared and Tau-squared will be used to measure heterogeneity.
To estimate publication bias, we will use funnel plot and Egger?s test. In addition to examining the risk of small-trial/publication bias with funnel plots, we will investigate the potential risk of bias due to selection of reported results within the risk of bias assessment and the potential risk of bias due to

selective non-reporting of results with the ROB-MEN(5) tool within the CINeMA assessment.
The standardized Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach will be used to examine the strength of evidence.

Project Timeline:

Start of project: The study will start immediately after the data is available.
The actual state of the project: it is planned to finish data extraction and to start data analysis by 11/2022. The manuscript will be made and submitted in six months (6/2023). The publication is planned for the following six months(12/2023).

Dissemination Plan:

The results of this work will be a significant advancement in optimizing antipsychotic treatment for psychiatric disease, which in turn will reduce the burden for patients with schizophrenia and their caregivers, as well as medical costs in the long term. We will make the results available in several publications in scientific journals (e.g., JAMA Psychiatry, Lancet Psychiatry). Moreover, it is expected that the results will be included in local and international treatment guidelines.

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