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SMRI-02T-162A: double blind placebo controlled trial of a protein kinase C inhibitor: tamoxifen citrate in treatment of acute mania

Submission date
07/12/2006

Registration date
28/12/2006

Last Edited
02/04/2008

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Mental and Behavioural Disorders

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00411203

Secondary identifying numbers
AY0001

Study information

Scientific Title

Acronym
Mania-Tamoxifen Trial

Study objectives
1.There will be greater reduction in ratings of manic or mixed mood symptoms with tamoxifen citrate compared to placebo.
2.A greater proportion of subjects will respond to tamoxifen citrate when compared to placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The study was approved by the Turkish Ministry of Health, General Directorate of Drugs and Pharmaceutics, Central Review Board, and Local Ethical Committee of Drug Investigations at the Dokuz Eylul University.

Study design
Randomised, controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Bipolar Disorder-I, most recent episode manic or mixed, with or without psychotic features

Interventions
Subjects were recruited from the local community, an urban area in the western part of Turkey, surrounding suburbs, and towns as well as all over the country (expert-seeking patients who reached the principle investigator [PI] via the internet and news media) between April, 2003 and June, 2006. All diagnoses were based on the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV), administered by a trained

investigator. After the protocol explained to the patient and at least one first degree relative, both gave written informed consent for participation of the patient in the trial. Subject screening included medical and psychiatric history, physical examination, and laboratory screen including Liver Function Tests (LFTs), Thyroid Stimulating Hormone (TSH), Human Chorionic Gonadotropin (HCG), Blood Urea Nitrogen (BUN), Creatinine, and serum toxicology. All psychotropic medication (except benzodiazepines) was discontinued at least one day before randomisation.

Subjects entering the study were randomly assigned to receive the Protein Kinase C (PKC) inhibitor, tamoxifen or identical placebo tablets in a 1:1 ratio and double-blind fashion for three weeks. Computer-generated codes were used to create randomisation kits (prepared by the ARGEFAR, a contract research organization). The starting dose of tamoxifen was 20 mg twice daily (bid). After the first treatment day, daily dose was adjusted upward by 10 mg per day up to 80 mg/d in divided doses. Similar tablet adjustments were applied for the patients in placebo group. Concomitant use of oral lorazepam (2.5 mg dissolving tables) was allowed during double-blind therapy as clinically indicated.

In cases where lorazepam is thought to be ineffective and the symptoms are such that an antipsychotic is required, risperidone liquid formulations (2-6 mg/day) were used under emergency circumstances. Those subjects who were given risperidone were assumed as drop out at the time of first exposure to risperidone; and new subjects for replacement of those cases have been recruited. Yet, the subjects who volunteer to continue study drug, assessed weekly without opening blind and data on combined use of open label risperidone and blind tamoxifen is presented in a separate section. Subjects were seen twice daily and investigators were on call 24 hours a day.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Tamoxifen citrate, lorazepam, Protein Kinase C (PKC) inhibitor, risperidone

Primary outcome measure
Assessment tools:
1. Young Mania Rating Scale (YMRS)
2. Hamilton Depression Rating Scale-17 item (HAMD-17)
3. Montgomery-Asberg Depression Rating Scale (MADRS)
4. Clinical Global Impressions-Bipolar Version of Severity of Illness (CGI)
5. Positive and Negative Syndrome Scale (PANSS) and side effect questionnaire

These were administered by semi-structured interviews at each week. Vital signs and weight were monitored. The PI, who is trained in the rating instruments and blind to the treatment condition (training and certification at the Massachusetts Hospital, Bipolar Program), performed all the study assessments on a weekly basis. The primary efficacy variable is defined as the reduction from baseline of the YMRS score after three weeks of therapy. Positive treatment response was defined as a more than 50% decrease in YMRS from baseline to three weeks.

Added as of 18/04/2007:
Analyses of all the primary and secondary outcomes were performed under the intent-to-treat principle based on normal linear mixed effect models based on all 66 randomised participants and all observations up until the time of drop out. Patients who initiated risperidone and dropped the study were included in the primary intent-to-treat analysis with their outcome scores censored at time of risperidone initiation.

Secondary outcome measures
The secondary outcome measures were the reductions from baseline of the PANSS and CGI Mania scores after three weeks of therapy.

Overall study start date
02/04/2003

Completion date
30/06/2006

Eligibility

Key inclusion criteria
1. Diagnosis of Bipolar Disorder (BD I), most recent episode, manic or mixed
2. Aged 18 to 65
3. Young Mania Rating Scale (YMRS) score more than 20 at screening and baseline
4. Providing written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Not Specified

Target number of participants
50

Key exclusion criteria
1. Currently pregnant, planning to become pregnant, or breast feeding
2. History of any coagulopathies, deep vein thrombosis, pulmonary embolus
3. A history of hypersensitivity to tamoxifen
4. Drug screen positive for any drug of abuse at screening, active substance abuse in the past two weeks or substance dependence in the past two months (except nicotine and caffeine)
5. Diagnosis of schizophrenia, dementia, delirium, seizure disorder, obsessive compulsive

disorder, or major cardiac, hepatic or renal disease that is unstable or that requires medical care
6. Administration of any other investigational drug in the last 30 days
7. Clinically significant suicidal or homicidal ideation

Date of first enrolment
02/04/2003

Date of final enrolment
30/06/2006

Locations

Countries of recruitment
Türkiye

United States of America

Study participating centre
McLean Hospital
Belmont
United States of America
MA 02478

Sponsor information

Organisation
The Stanley Medical Research Institute (SMRI) (USA)

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Sponsor type
Research organisation

Website
http://www.stanleyresearch.org

ROR
https://ror.org/01pj5nn22

Funder(s)

Funder type
Research organisation

Funder Name
Stanley Medical Research Institute (SMRI) (USA) (Grant ID: 02T-162A)

Alternative Name(s)
The Stanley Medical Research Institute, SMRI

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Results	01/03/2008		Yes	No