



UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM

FACT SHEET

Studies Involving Placebo-Only Treatment in High Risk Patients with Psychiatric Illness

A workgroup of the UCSD Department of Psychiatry, at the request of the Human Research Protections Program, reviewed and updated guidelines for the safe and ethical conduct of studies involving High Risk Patients with Psychiatric Illness in October, 2004.

For the purpose of these guidelines, the workgroup defined "High Risk Patients" as patients diagnosed with a major psychotic illness such as schizophrenia, bipolar disorder, or schizoaffective disorder. These diagnosis fall into the category of psychiatric disorders that the Department of Veteran Affairs refers to as "Significant Mental Illness". These guidelines should be followed when preparing research study applications to the UCSD Human Research Protections Program (HRPP).

Guidelines

In general, subjects who are assigned to a potential placebo-only treatment trial should be observed in a closely supervised inpatient or residential (in house) crisis center during the high-risk period. If the protocol allows for subjects to be discharged after the high-risk period then the following criteria should be addressed in the UCSD HRPP application.

1. Subjects have been observed as an inpatient for at least 1 week after being randomized to potential placebo-only treatment (no less than 1 week) to determine that they are tolerating study medication well and are reliably compliant with treatment and showing no evidence of worsening of symptoms. This must be reflected in each subject's medical chart.
2. Subjects will be free of active self-harm ideation or behavior for at least 1 week before discharge and this is documented in each subject's medical record.
3. Subjects will meet objective criteria (e.g. based upon the rating tools being used in the study such as PANSS, BPRS, YMRS, CGI, etc. developed by the PI and approved by the review committee) that the subject is appropriate to be discharged and to continue the study as an outpatient.
4. The subject's appropriateness to continue participation in the study as an outpatient will be independently assessed by two qualified psychiatrists and/or psychologists not connected to the study and formally documented in the subject's medical chart.
5. Prior to discharge the subject must identify an individual (close friend or relative) who sees him/her on a daily basis and who consents to act as a contact person. The subject must be willing to be monitored by the contact person and be willing to have the study staff and contact person regularly communicate about the subject's safety and appropriateness to continue in the study.

The contact person will be educated by study staff regarding what symptoms and behaviors to look for which may indicate a worsening in the subject's illness and represent a potential risk to the subject's safety. The contact person must be willing to contact the study staff should he/she see evidence of such symptoms or behaviors or if the subject appears not to be compliant with medication, expresses concerning thoughts or plans, leaves his/her stable place of residence, or engages in

behavior that is contrary to the study and/or may potentially worsen the illness (e.g. illicit drug use). The contact person must agree that the subject is ready for discharge. This agreement will be formally documented in the subject's medical chart.

6. Subjects must have an identified stable place of residence where they can be contacted by telephone and where the contact person can monitor him/her. This must be in the Contact Person Consent Form and approved by a UCSD Institutional Review Board (IRB).
7. Prior to discharge, the study staff will provide the subject and the contact person written instructions about the study including the name of the study and the PI, the manner in which study medication/s are to be taken, the dates and location of follow-up visits, and phone numbers where the subject can reach study staff 24 hours per day for questions and emergencies. A copy of these instructions will be placed in the subject's chart.
8. A plan must be submitted and approved by the IRB that details how the research staff will follow the subject, and must include the following: information on frequency of follow-up assessments, the plan if the subject does not show up for a scheduled visit, and the plan if the subject cannot be reached by study staff or the contact person.
9. An outline must be provided which delineates the criteria to be used in determining that the subject is no longer appropriate for the study. For example, most multi-site pharmaceutical industry-sponsored studies allow subjects to be discontinued if "in the judgment of the principal investigator" continuing in the study would be harmful and/or inappropriate for the subject. This outline must provide specific, objective criteria (e.g. based upon the rating tools being used in the study such as PANSS, BPRS, YMRS, CGI, etc.) to be used in

determining whether a subject who is potentially on placebo-alone treatment should be discontinued from a study due to evidence of worsening or lack of improvement in symptoms.

10. A plan must be provided for rescue of a subject who has significantly worsened during the course of the study and is now at greater risk. Elements in this plan should include a mechanism for hospitalizing patients readily, and/or discontinuing patients from study medication and restarting standard treatment. How the costs will be covered for stabilizing such a subject should be addressed. Note that it is UCSD policy in sponsored studies that the sponsor, not the subject or the subject's insurance provider, covers all reasonable costs for patients who need stabilization treatment.

Additional Follow up Visit Criteria

The research plan should include the provision that study staff will make frequent follow-up assessments of subjects who are enrolled in placebo-alone controlled studies as outpatients. During these follow-up assessments the following should be documented:

1. Subject's relevant psychiatric symptoms;
2. Subject's ongoing appropriateness to continue as an outpatient in study based upon criteria 1 – 10 above;
3. Evidence that the subject maintains his/her consent to continue participating in the study and is competent to do so;
4. Status of the contact person.

Criteria for Termination of Participation

The research plan should include the provision that the PI will make available for a subject who leaves the study a means for him/her to safely discontinue study medication and receive appropriate follow-up treatment.

The following must also be addressed in placebo-alone controlled studies:

1. If subjects are being taken off their medication, the consent must clearly state that they will be on no medication (placebo alone and/or washout period) for a portion of the study. The number of weeks that a subject may be on an investigational drug must be specified, and it must be clear that this drug may not control their illness. It must be explicitly stated that there is a good chance that their disease may worsen during the trial.
2. A subject's capacity to consent must be objectively demonstrated. Study staff must submit a copy of the assessment tool that will be used to determine the subject's understanding of key elements of the study protocol, including design, risks, expectations and alternatives. Further information on decisional capacity assessment is available at <http://irb.ucsd.edu/decisional.shtml>

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