Appendix G: Study Announcement

The Feinstein Institutes for Medical Research and Cohen Children's Medical Center Announce the Addition of Boston Children's Hospital as a Study Center for the Clinical Trial of Trifluoperazine for Transfusion-Dependent Adult Patients with Diamond Blackfan Anemia

Dear DBA Patients and Families:

We are pleased to announce that Boston Children's Hospital is another site for the DBAR TFP trial **"Phase I/II, Open-Label Study to Determine Safety of Trifluoperazine (TFP) in Adults with Red Blood Cell Transfusion-Dependent Diamond Blackfan Anemia".**

Diamond Blackfan Anemia (DBA) is a rare pure red cell anemia resulting from a failure of the bone marrow to make red blood cells. The anemia may present in infancy, in childhood, or occasionally in adulthood. For some patients a genetic cause for DBA can be found but for others no known genetic mutation is known at this time. Some patients have little or no anemia after treatment with steroids, whereas others may need continuous red blood cell transfusions or steroid therapy for a long time, sometimes for life. Steroids may control DBA in many patients at first, but after some time, the steroids may not work as well anymore. Unfortunately red cell transfusions have many possible negative side effects, such as iron overload. Iron overload can occur in the liver, heart, and endocrine organs which can cause more complicated health problems such as liver or heart failure, diabetes, thyroid issues, gonadal dysfunction, etc.

Purpose of this study
The purpose of this study is to find an alternative treatment for patients with DBA who are dependent upon transfusions. This study uses a medication called trifluoperazine (TFP) and determines if it is safe for the treatment of DBA in adult patients who require chronic blood transfusions. This is a research study because TFP has never been tested in patients with DBA. TFP is a drug that has been approved by the Food and Drug Administration (FDA) for the treatment of psychiatric disorders. TFP has not been previously approved by the FDA for treatment of DBA. In this research study the safety of TFP is being tested at different dose levels in patients with DBA. A total of 24 patients with DBA may be enrolled on this study.

About the study drug, Trifluoperazine or TFP
TFP is a typical oral antipsychotic medication that has been used for the treatment of psychiatric patients since 1958. In the United States, TFP is approved for the short-term treatment of anxiety; treatment or prevention of nausea and vomiting of various causes; and management of psychotic disorders. In part because of its side effect profile, TFP has been largely replaced by second and third generation anti-psychotic medications. Nevertheless, TFP remains commercially available worldwide and the risks associated with its use are well understood and generally manageable.

Description of procedure
The study is 29 days long and consists of taking the study drug TFP for 21 days and being monitored for an additional 8 days. The patient will have 4 study visits over the period of 29 days. A review of the patient's history, physical examination, and laboratory blood work will be

done in order to determine if the patient is eligible to participate. The patient will start the TFP on Day 1 of the study period. While the patient is taking the TFP, he or she will need to be seen at the Feinstein Institutes or at Boston Children's Hospital on Day 11 and on Day 22. The final visit on Day 29 may be at the study center or at the patient's primary physician/hematologist. During the first 21 days the patient will be taking TFP once a day, orally as a tablet, and will continue the red blood cell transfusions as routinely scheduled, every 3-4 weeks.

The following are some of the basic inclusion and exclusion criteria for this pilot trial.

Inclusion Criteria

- Diagnostic and supporting criteria for the diagnosis of DBA
- Transfusion dependence every 3-4 weeks
- Age greater than or equal to 18 years and less than 65 years
- Weight greater than or equal to 45 kilograms or 99 lbs
- Negative pregnancy test
- Signed informed consent

Exclusion Criteria

- Have a known allergy to TFP or other phenothiazines (class of drugs including TFP)
- Evidence of kidney or liver dysfunction
- Evidence of heart disease or history of angina
- Uncontrolled high blood pressure
- Pregnancy, or plan to become pregnant during duration of trial
- History of cancer

Please refer to the website link: http://www.clinicaltrials.gov and enter the search term "Diamond-Blackfan Anemia and trifluoperazine" for full eligibility criteria and additional trial information.

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