

Dear Referring Cardiologist/Geneticist:

I would like to introduce you to an exciting new research study, "**The Marfan Trial,**" a Trial of Beta Blocker Therapy (Atenolol) vs. Angiotensin II Receptor Blocker Therapy (Losartan) in individuals with Marfan syndrome (MFS). This trial is being conducted under the auspices of the Pediatric Heart Network (PHN), a multi-center clinical research network funded by the National Heart, Lung, and Blood Institute, NIH/DHHS. The Marfan Trial is being conducted at the eight Network clinical centers, as well as up to 12 additional sites. The major aims of this multi-institutional, randomized clinical trial will be to compare aortic root growth and other short-term cardiovascular outcomes between subjects receiving either atenolol or losartan.

As you know, MFS is a systemic disorder of connective tissue with autosomal dominant inheritance and a population prevalence of approximately 1 per 5,000. Cardiovascular pathology, including aortic root dilation, dissection, and rupture is the leading cause of mortality in the MFS. Several studies have shown that beta blockers (BB) reduce the rate of aortic growth. Although advances in therapy have improved life expectancy, individuals with MFS continue to suffer significant cardiovascular morbidity and mortality. Recent studies in a *FBN1*-deficient mouse model of MFS with a susceptibility to aortic dilation and dissection, similar to that seen in humans with MFS, showed that postnatal treatment with losartan, an angiotensin II receptor blocker (ARB), normalized aortic root growth and aortic architecture, preventing aortic aneurysms and premature death [Habashi JP et al: Losartan, an AT1 antagonist, prevents aortic aneurysm in a mouse model of Marfan syndrome. *Science* 2006;313:117-121].

Clearly, a prospective, randomized trial is necessary to determine whether the promising results seen in the mouse model will also be seen in humans with MFS. We hope to have your support in enrolling your patients. A word of encouragement from the referring cardiologist/geneticist is of utmost importance, not only for the families' comfort with routine care, but also for their willingness to participate in the study.

Attached is an outline of the highlights of the protocol. We would be more than happy to visit your practice to discuss the rationale for the study and the details of the protocol, and to answer any questions personally.

You may also refer to the PHN Web site (www.pediatricheartnetwork.com) for additional information.