

# **Trial of Beta Blocker (BB) Therapy (Atenolol) vs. Angiotensin II Receptor Blocker (ARB) Therapy (Losartan) in Individuals with Marfan Syndrome**

## **Marfan Study Summary**

### **Study Design**

A Phase III, randomized, multi-center trial to compare the effect of atenolol therapy to that of losartan therapy on rates of aortic growth and progression of aortic regurgitation in individuals with Marfan syndrome (MFS). Subjects are followed for three years after randomization. The target number of participants is 604. The accrual period is approximately 6 years with recruitment to begin in January 2007.

### **Primary Endpoint**

Rate of change in aortic root Z-score, adjusted for body surface area.

### **Secondary Endpoints**

- Frequency of combined endpoint: aortic dissection, aortic root surgery or death
- Rate of change of mitral regurgitation
- Rate of progression of left ventricular dilation and dysfunction
- Rate of change in central aortic stiffness indices
- Long bone overgrowth and weight gain
- Comparison of adverse drug reactions between groups

### **Inclusion Criteria**

- 6 months to 25 years of age
- Diagnosis of MFS according to Ghent criteria
- Aortic root Z-score >3.0

### **Exclusion Criteria**

- Prior aortic surgery
- Aortic root dimension at the sinuses of Valsalva >5 cm.
- Planned aortic surgery within 6 months of enrollment
- Aortic dissection
- Shprintzen-Goldberg syndrome
- Loeys-Dietz syndrome
- Therapeutic rather than prophylactic use of ACE-I, BB, or calcium channel blocker (e.g. for arrhythmia, ventricular dysfunction or valve regurgitation)
- History of angioedema while taking ACE-I or BB
- Intolerance to losartan or other ARB that resulted in termination of therapy
- Intolerance to atenolol or other BB that resulted in termination of therapy
- Renal dysfunction
- Asthma of sufficient severity to preclude use of a BB
- Diabetes mellitus
- Pregnancy or planned pregnancy within 36 months of enrollment
- Inability to complete study procedures including history of poor acoustic windows (inability to obtain accurate measurement of aortic root)