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UPDATE ON THE HOUSTON METHODIST DEBAKEY HEART & VASCULAR CENTER CARDIAC STEM CELL STUDIES

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Despite current treatment, heart failure is a contributing factor in approximately 15 million deaths worldwide each year. Currently available treatment options include medical management, cardiac transplantation, ventricular assist device therapy, and investigational therapies such as stem cells. The majority of cardiac stem cell therapy has been performed in other countries using direct surgical injection or catheter delivery systems. Early phase trials have been completed in the United States and include surgery or catheter delivery. Although these trials have focused primarily on safety, efficacy, including cardiac improvement, has been recorded. The exact mechanism explaining why some patients demonstrate improvement is still unknown, but it may involve stimulation of angiogenesis or paracrine factors and remodeling at the cellular level.

At the Houston Methodist DeBakey Heart & Vascular Center, we have recently finished two phase II multicenter trials evaluating direct injection of stem cells into failing myocardium in heart failure patients. The first trial, sponsored by Aastrom Biosciences (IMPACT-DCM), involved direct injection of the patient's own bone marrow-derived stem cells into the left ventricle during a surgical procedure. A small left anterior thoracotomy incision was used while the patient was under general anesthesia. Forty total patients across the country were enrolled in this trial, and our center was one of the highest enrolling, with five treated patients and three control patients. The trial recently completed the last patient 6-month follow-up. Preliminary data analysis revealed that the stem cells were safe, and significant improvements in functional status (i.e., New York Heart Association status, 6-minute

walk distance) were noted in a small cohort of patients with ischemic cardiomyopathy. Further data analysis is ongoing, and the company has recently started a catheter-based arm of this study. Using radiologic guidance, the stem cells are now delivered through a catheter system placed directly into the heart from a groin approach. Our center is slated to start enrolling patients in the upcoming months.

The second study, which we recently completed, was a phase II multicenter trial (HARVEST CABG trial) involving direct injection of the patient's stem cells into the failing myocardium during coronary artery bypass surgery. We treated two patients in this study, including one control patient. Preliminary analysis reveals the stem cell product to be safe, and the effects on cardiac function, including the patient's quality of life, are being analyzed.

As we look to the future, the Houston Methodist DeBakey Heart & Vascular Center plans to continue its collaboration with stem cell companies and participate in upcoming multicenter prospective trials, including phase III studies. What we know so far is that bone marrow derived stem cells appear to be safe when injected into the heart, and further studies focused on efficacy are ongoing.

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