Results From the EVEREST II Trial

Percutaneous mitral valve repair using the MitraClip System is a safe and effective treatment for patients with significant mitral regurgitation (MR). Two established strategies for the treatment of significant MR are medical management, which controls symptoms but does not address underlying pathophysiology or disease progression, and surgical repair or replacement, which is effective but invasive. Thus far, there is an unmet need for a less invasive treatment option, particularly among the elderly and in the presence of comorbidities. Ted E. Feldman, MD, Evanston Hospital, Evanston, IL, presented findings from the Endovascular Valve Edge-to-Edge Repair Study (EVEREST II; NCT00209274), which investigated a noninvasive mitral repair option for MR.

EVEREST II was a randomized, multicenter, controlled trial that included 279 patients (MitraClip Device, n=184; Control of Surgical Repair/Replacement, n=95) with moderate to severe (3+) or severe (4+) MR according to American College of Cardiology/American Heart Association guidelines who were candidates for mitral valve surgery. Patients in both groups were well matched at baseline. It is important to note that 73% of patients had degenerative MR and 27% of patients had functional MR in both groups.

The primary safety endpoint was major adverse event (MAE) rate at 30 days using a superiority hypothesis and per-protocol cohort. The primary effectiveness endpoint was clinical success rate or freedom from the combined outcome of death, mitral valve surgery or reoperation for mitral valve dysfunction, or MR >2+ at 12 months using a noninferiority hypothesis and per-protocol cohort. Additional analyses included intention-to-treat (ITT) for safety (MAE rate at 30 days) and effectiveness (freedom from composite of death, mitral valve surgery > 90 days or reoperation for mitral valve dysfunction >90 days postindex procedure, or MR >2+ at 12 months) and clinical benefit assessment using MR severity, left ventricular function, NYHA Functional Class, and quality of life (SF-36) survey as measures of clinical benefit.

The MitraClip device demonstrated superiority over control with regard to safety (p<0.0001). MAEs were observed in 9.6% of patients in the device group compared with 57.0% in the control group, an observed difference of 47.4% at 30 days (Table 1). Additionally, the MitraClip device was noninferior to control with regard to clinical success rate at 12 months (72.4% for the device group vs 87.8% for the control group; p=0.0012). Results of the safety and clinical success rates in the ITT analysis were similar to those of the per-protocol cohort. The device group demonstrated safety superiority (p<0.0001) and effectiveness noninferiority (p=0.0005) compared with control in the ITT analysis.

Table 1. EVEREST II - 30-Day MAEs.

30 Day MAE, non-hierarchical	# Patients experiencing event	
	Device Group (n=136)	Control Group (n=79)
Death	0	2 (2.5%)
Major Stroke	0	2 (2.5%)
Re-operation of Mitral Valve	0	1 (1.3%)
Urgent/Emergent CV Surgery	0	4 (5.1%)
Myocardial Infarction	0	0
Renal Failure	0	0
Deep Wound Infection	0	0
Ventilation >48 hrs	0	4 (5.1%)
New Onset Permanent AF	0	0
Septicemia	0	0
GI Complication Requiring Surgery	1 (0.7%)	0
All Transfusions ≥2 units*	12 (8.8%)	42 (53.2%)
Total % of Patients with MAE	9.6%	57.0%
	p<0.0001* (95% CI, 34.4% to 60.4%)	
*p<0.0001 if include major bleeding only		

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Clinical benefit was observed in the MitraClip and mitral valve surgery patients through 12 months. These patients demonstrated improvements in left ventricular function, NYHA Functional Class, and quality of life.

Based on these findings, the MitraClip procedure may be a feasible therapeutic option for selective patients with significant mitral regurgitation, and surgery remains an option after MitraClip procedure. Results from EVEREST II are promising with regard to safety, efficacy, and clinical benefit. However, MitraClip is an investigational device only and is not currently available for sale in the United States.

The Safety and Tolerability of Betrixaban Therapy

The oral direct factor Xa inhibitor betrixaban, at doses of 40 mg, 60 mg, and 80 mg once daily, is safe and well tolerated compared with dose-adjusted warfarin in patients with nonvalvular atrial fibrillation (AF) or atrial flutter. Michael D. Ezekowitz, MD, PhD, Vice President, Lankenau Institute for Medical Research, Thomas Jefferson Medical College, Wynnewood, PA, presented results from the Phase II, randomized, multicenter EXPLORE-Xa Trial (NCT00742859).