Transcatheter Mitral Valve Repair System
Early Feasibility Study Protocol

Device Name:

Dragonfly-M™ Transcatheter Mitral Valve Repair System

Version: V1.0

Date: June 8th, 2020

Protocol Synopsis

Protocol name: Dragonfly-M™ Transcatheter Mitral Valve Repair System – Early Feasibility Study Protocol

Objectives: To evaluate the safety and device performance of the Dragonfly-M™ transcatheter mitral valve repair system for the treatment of moderate-to-severe or severe mitral regurgitation in high or prohibitive surgical risk subjects. This trial is designed to study the reliability and operator performance of the Dragonfly-M™ transcatheter mitral valve repair system in an early feasibility study.

Trial products: Dragonfly-M™ Transcatheter Mitral Valve Repair System

Indications: Moderate-to-severe (3+) and severe (4+) mitral regurgitation in high or prohibitive surgical risk subjects.

Trial design: The subjects with moderate-to-severe (3+) and severe (4+) mitral valve regurgitation (MR) at high or prohibitive surgical risk will be evaluated by the study sites, and study eligibility confirmed by the echocardiographic core laboratory and eligibility committee. Those qualifying will then be treated with Dragonfly-M™ transcatheter mitral valve repair system after signing the informed consent. The follow-up will be conducted at discharge, 30 days, 6 months and 12 months after the operation. The primary endpoints are the incidence of major adverse events (MAE) at 30 days, and acute procedural success. Acute procedural success is defined as placement of one or more Dragonfly-M™ devices on the mitral valve with reduction of MR to 2+ or less. The secondary endpoints include all-cause mortality, cardiovascular mortality, incidence of serious adverse event, cardiovascular rehospitalization, NYHA functional class, mitral valve hemodynamics, acute technical success rate and device success rate at 6 months. Acute technical success is defined as no procedural mortality, successful in access, delivery, and retrieval of the device delivery system, and no emergency surgery or reintervention related to the device or access procedure in the catheterization laboratory. Device success is defined as no procedural mortality, proper delivery and deployment of the device, no unplanned surgical or interventional procedures related to the device, no specific device-related technical failure and or complications, function improvement of MR without significant stenosis (MR $\leqslant$ 2+) and without associated hemolysis or thrombogenesis.

Follow-up duration: Follow-up will be conducted at discharge, 30 days, 6 months and 12 months after operation.

Inclusion criteria:

1. Age ≥ 18 yrs
2. Moderate–to-severe (3+) or severe (4+) mitral valve regurgitation on transthoracic or transesophageal echocardiography, and confirmed by echocardiographic core laboratory
3. The patient is on optimal guideline directed medical therapy for heart failure and remains symptomatic.
4. High or prohibitive surgical risk as defined by either Society for Thoracic Surgery Risk Calculator score for valve replacement ≥ 8 points; or STS score for valve repair ≥ 6 points , prohibitive risk as determined by the clinical judgement of the site heart team, including a cardiac surgeon experienced in mitral valve surgery and a cardiologist experience in mitral valve disease, due to the presence of one or more documented surgical risk factors.
5. Anatomically suitable for mitral valve repair and can be treated by Dragonfly-M^{TM} confirmed by both site investigators, echocardiographic core laboratory, and the eligibility committee.
6. Transseptal catheterization and femoral vein access is determined to be feasible
7. Life expectancy ≥ 12 months
8. The subject or the subject's legal representative has been informed of the nature of the trial, willing to accept the experimental tests and follow-ups, and has provided written informed consent

Exclusion criteria:

1. History of heart transplantation, prior mitral valve replacement surgery. or transcatheter mitral valve procedure;
2. Leaflet anatomy which may preclude Dragonfly-M^{TM} implantation and position, as judged by the site investigators and confirmed by the echocardiographic core laboratory and eligibility committee
3. Evidence of calcification or significant cleft in the grasping area
4. LVEF < 20%
5. LVESD≥ 60mm;
6. Mobile leaflet length＜10mm

7. Mitral valve effective orifice area (EOA) < 3.5cm2 or in the opinion of site investigators and confirmed by the echocardiographic core laboratory and eligibility committee that mitral stenosis would result from implantation of the Dragonfly-M^{TM} device.
8. Echocardiographic evidence of intracardiac mass, thrombus or vegetation;
9. Severe non-mitral valve disease requiring treatment .
10. Severe pulmonary artery hypertension (sPAP＞70mmHg)
11. Severe right ventricular dysfunction;
12. Active endocarditis or previous mitral valve endocarditis; Active rheumatic heart disease or leaflets degenerated from rheumatic disease
13. Severe untreated coronary artery stenosis requiring revascularization; or with other cardiovascular disease requiring surgical treatment；
14. Extreme frailty
15. Hypertrophic cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis and any other structural heart disease causing heart failure other than dilated cardiomyopathy;
16. Renal failure requiring dialysis;
17. Blood cachexia including granulocytopenia (WBC < 3×109/L), acute anemia (HB < 90g/L), thrombocytopenia (PLT < 50×109/L), severe coagulopathy, and contradictions of anticoagulant and antiplatelet agents;
18. Evidence of an acute myocardial infarction in the prior 4 weeks;
19. Evidence of a shock in the prior 90 days;
20. Any percutaneous cardiac intervention or carotid surgery or any cardiac surgery within the 30 days prior to randomization;
21. Evidence of acute peptic ulcer upper or gastrointestinal hemorrhage in the prior 90 days;
22. Severe symptomatic carotid artery stenosis over 70% confirmed by echocardiography;
23. The subjects suffer from diseases which may lead difficulty in evaluating treatment (e.g., cancer, infection, severe metabolic disease, psychosis, etc.); or special cases that were evaluated by the heart team of local experimental center as not suitable for the surgical application of this clinical trial;
24. Life expectancy ≤ 12 months;

25. Subject participating in an investigational drug or another device study within the past 1 month;
26. In the judgment of the investigator, subjects may not complete the trial according to poor compliance.

Primary Effectiveness Endpoint:

1) Incidence of major adverse event (MAE) at 30 days

   Major adverse event is defined as one of the following components: death, myocardial infarction (MI), stroke, renal failure requiring dialysis, and cardiac surgery for Dragonfly-M^{TM} device failure.

2) Acute procedural success

   The acute procedural success is defined as successful Dragonfly-M^{TM} implantation, and residual MR of 2+ or less at discharge. An echocardiogram at 30 days can be accepted if the discharge image was not available or hard to interpret. A death before discharge or a re-operation of mitral valve prior to 30 days is defined as acute procedure failure

Secondary Effectiveness Endpoints:

1. All-cause mortality (frame:6 months)
2. Cardiovascular mortality (frame:6 months)
3. Incidence of serious adverse event (SAE）(frame:6 months). If the adverse event meets any of the criteria below, it is regarded as a serious adverse event (SAE): 1) results in death; 2) is life threatening, results in illness or injury; 3) requires inpatient hospitalization or prolongation of existing hospitalization; 4) results in a persistent or significant disability/incapacity; 5) results in a congenital anomaly/birth defect, fetal death, fetal distress; 6) results in medical or surgical intervention to prevent permanent impairment to body structure or a body function; 7) an important medical event that may not result in death, be life-threatening, or require hospitalization but may be considered serious when, based upon appropriate medical judgment, may jeopardize the patient or subject and/or may require intervention to prevent one of the outcomes listed in this definition.
4. Incidence of cardiovascular rehospitalization (frame:6 months)
5. NYHA functional class (frame:6 months)
6. Mitral valve hemodynamics (frame: 6 months): include residual mitral regurgitation degree, and mean mitral valve gradient.

7. Technical success (frame: in the catheterization laboratory): must meet all of the following items: 1) no procedural mortality; and 2) successful in access, delivery, and retrieval of the device delivery system; and 3) no emergency surgery or reintervention related to the device or access procedure.
8. Device success (frame: 6 months): must meet all of the following items:1) No procedural mortality; 2) Proper delivery and deployment of the device; 3) No unplanned surgical or interventional procedures related to the device; 4) No specific device-related technical failure or complication. 5) Improvement of MR without significant stenosis (MR ≤ 2+) without associated hemolysis or thrombogenesis.

Sample size: 20 cases

Clinical evaluation schedule:

Items	Screening/ Baseline	During procedure	Follow up			
			discharge	1month	6month	12months
Time frame	-14d to 0d	0	-	±14d	±30d	±45d
Informed consent	X					
Eligibility criteria	X					
Medical history	X					
Physical examination	X					
Vital signs	X	X	X			
12 lead ECG	X		X			
Transesophageal echocardiogram	X[1]	X				
Transthoracic echocardiogram	X[1]		X	X	X	X
Complete blood count[2]	X		X			
Renal function test[3]	X		X			
CK/CK-MB / BNP	X		X			
NYHA Functional class	X		X	X	X	X
Device performance evaluation		X				
Medication[4]	X	X	X	X	X	X
Adverse events[5]		X	X	X	X	X

Note:

1. TTE within 45 days and TEE within 120 days prior screening frame can be accepted.
2. Complete blood count includes: RBC, WBC, PLT, Hb
3. Renal function test include serum creatinine and urea nitrogen
4. For medication, only anticoagulation drugs and antiplatelet drugs are recorded
5. Adverse events include adverse events, severe adverse events and complications.