Transcatheter Mitral Valve Repair System Early Feasibility Study Protocol

Device Name:

SQ-Kyrin™ Transcatheter Mitral Valve Repair System

Version: V1.0

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Protocol Synopsis

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Background: Mitral regurgitation (MR) is the reflux of blood flow from the left ventricle to the left atrium during systole due to mitral valve insufficiency, and its incidence gradually increases with age. Large-scale epidemiological surveys in the United States have found that about 9.3% of the population over 75 years of age and 6.4% of the population aged 65–74 years suffered from MR, and its incidence is about five times that of aortic stenosis. Although there are currently a large population of about 2.5 million patients with moderate/severe MR in the United States, only 2% of the patients receive surgical treatment, 49% of MR patients do not receive surgery for high surgical risks caused by low cardiac function, many complications, advanced age and other factors, and 49% of MR patients do not visit the hospital and are not treated. Although there is no large-scale epidemiological survey in China, according to the statistical calculation of some single centers, there are about 10 million patients with moderate to severe MR requiring treatment in China. Moreover, with the aggravation of the aging population, the number of patients will continue to grow. However, the current volume of mitral valve surgery in China is only 40,000 cases/year, and the vast majority of patients are still not effectively treated. Studies have shown that patients diagnosed with severe MR without surgery can lead to progressive left ventricular dysfunction and congestive heart failure, seriously affecting the life quality of patients. Generally, the mortality rate is 20% after one year of diagnosis and 50% after five years of diagnosis. The probability of admission for secondary heart failure is as high as 90%, bringing serious medical burden to the society

Objectives: A feasibility study to evaluate the effectiveness and safety of the Transcatheter Edge-to-Edge Valve Repair System for the treatment of moderate-to-severe mitral regurgitation in patients with high surgical risk

Trial products: SQ-Kyrin™ Transcatheter Mitral Valve Repair System

Indications: This product is suitable for patients with moderate to severe degenerative or functional mitral regurgitation. Patients need to be clinically evaluated to determine that they are at high risk from traditional surgery, or cannot tolerate traditional open thoracic surgery, and traditional

medical treatment cannot reverse organic heart disease

Trial purpose: A clinical validation is to be performed to evaluate the performance (operability) and reliability of the SQ-Kyrin™ Transcatheter Edge-to-Edge Valve Repair System of Shanghai Shenqi Medical Co., Ltd. in treating moderate-to-severe degenerated mitral regurgitation (degenerated MR) and functional mitral regurgitation (functional MR) in Chinese population with high or prohibitive risk for conventional surgery

Trial design: This is a prospective, multicenter, single-arm observation, feasibility clinical study that plans to enroll a total of not less than 10 and not more than 30 patients, adopts the post-op immediate technical success rate as the primary endpoint, and uses the all-cause mortality at 30 days post-op, incidence of serious adverse event at 30 days post-op, device success rate at 30 days post-op, and procedural success rate at 30 days post-op as secondary endpoints to evaluate the effectiveness, safety, and feasibility of the Transcatheter Edge-to-Edge Valve Repair System of Shanghai Shenqi Medical Technology Co., Ltd. in clinical use and preliminarily evaluate the product's performance. A phasic study report (for phasic data summary and analysis) will be issued after completion of the 30-day postoperative follow-up to evaluate the effectiveness, safety, and feasibility of the device and apply for clinical studies before official registration and marketing. In the meantime, patients enrolled will continue to be followed up for 6 months and 1-5 years post-op to evaluate the long-term effect of the mitral valve repair system

Inclusion criteria:

1. Severe mitral valve regurgitation ≥ 3+ (moderate-to-severe mitral regurgitation disease);

2. Patients with high or prohibitive risk for conventional open thoracic surgery as defined by STS risk scoring result; subjects who are judged as not tolerating mitral valve surgery due to STS procedural mortality risk ≥ 8% for mitral valve replacement or presence of any of the following risk factors:

   a. Porcelain aorta or active ascending aortic atheroma

   b. Prior radiation therapy to mediastinum

   c. History of mediastinitis

   d. Left ventricular ejection fraction (LVEF) < 40%

   e. Presence of unobstructed coronary artery bypass graft

   f. History of 2 or more cardiothoracic surgeries

g. Liver cirrhosis

h. Other surgical risk factors

3. Degenerated MR patients, or functional MR patients who have received guideline-directed medical therapy (GDMT therapy)

4. Age ≥ 18 years, male or female;

5. Patients who are at extremely high risk or not suitable for conventional mitral valve surgery, as assessed by a multidisciplinary heart team (including at least one cardiac surgeon and one cardiologist);

6. Anatomically suitable for transcatheter mitral valve repair by edge-to-edge technique and can be treated by the SQ-Kyrin™ device;

7. Patients who can understand the objectives of the trial, volunteer to participate in the study, sign the informed consent form, and are willing to receive related examinations and clinical follow-up. laboratory and the investigator through discussion

Exclusion Criteria:

1. History of cardiac and mitral valve surgeries;

2. Infective endocarditis or evidence of active infection;

3. Mitral valve stenosis;

4 Severe uncontrolled coronary artery disease;

5. Pulmonary artery hypertension (systolic pulmonary artery pressure > 70 mmHg);

6. Severe right cardiac insufficiency;

7. LVEF < 30%;

8. Cardiac function of NYHA Class IV;

9. Patient is extremely week to tolerate surgery under general anesthesia, or in a shock state indicating circulatory support;

10. Hypertrophic cardiomyopathy, restrictive cardiomyopathy, or constrictive pericarditis;

11. Chronic dialysis;

12. Definite coagulation disorder and severe coagulation system diseases;

13. Clear contraindications for use of anticoagulants;

14. Cerebral stroke or transient ischemic attack in the past 30 days;

15. Any cardiac mass, left ventricular or atrial thrombosis identified by echocardiography;

16. Other valve diseases that requiring surgery or intervention;

17. Severe macrovascular disease requiring surgical treatment;

18. Treatment-naive carotid artery stenosis > 70%;

19. Imaging evidence of inappropriate cardiac and valve anatomy;

20. Known hypersensitivity to contrast media, and nickel-titanium memory alloy products;

21. Severe nervous system disorder compromising the cognitive ability;

22. Life expectancy < 12 months;

23. Severe thorax deformity;

24. Pregnant and lactating women.

Primary Endpoints:

1.Incidence of acute procedural success (Immediate postoperative)

Must meet all the four items：

1）No procedural mortality;

2）Success in delivery and retrieval of the device delivery system;

3）Successful deployment and accurate positioning of the device;

4）No emergency surgery or reintervention related to the device or surgical approach

Secondary Endpoints:

1. All-cause mortality at 30 days post-op

2. Incidence of serious adverse event at 30 days post-op;

3. Device success rate[1] (30 days post-op);

4. Procedural success rate[2](30 days post-op)

[1] Definition of device success: must meet all the four items below

1. No procedural mortality or stroke

2. Proper deployment and positioning of the device

3. No emergency surgery or reintervention related to the device or surgical approach

4. The implanted mitral valve repair system achieves the following safety and effectiveness indicators:

– No evidence of structural or functional abnormality

– No device-related technical failure or complication

– Significant functional improvement after valve repair, without significant stenosis (post-op EOA ≥ 1.5 cm^2 and transvalvular pressure gradient < 5 mmHg/valve regurgitation ≤ Grade 2+/no device-related hemolysis)

[2] Definition of procedural success: must meet the two items below

1. Device success

2. Absence of the following severe complications: death; stroke; life-threatening hemorrhage; severe vascular complications; secondary severe organic heart diseases (e.g.: aortic dissection, left atrium/auricle rupture, left ventricular outflow tract obstruction, etc.); Grade II-III and above renal insufficiency; myocardial infarction or coronary ischemia requiring percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG); severe hypotension, heart failure, respiratory failure requiring use of high-dose vasoactive medications/mechanical acids; any valve-related dysfunctions, including repair device detachment (single or two valve leaflets)/embolism/device-related autologous mitral valve damage/other conditions requiring second intervention

Sample size: 20 cases