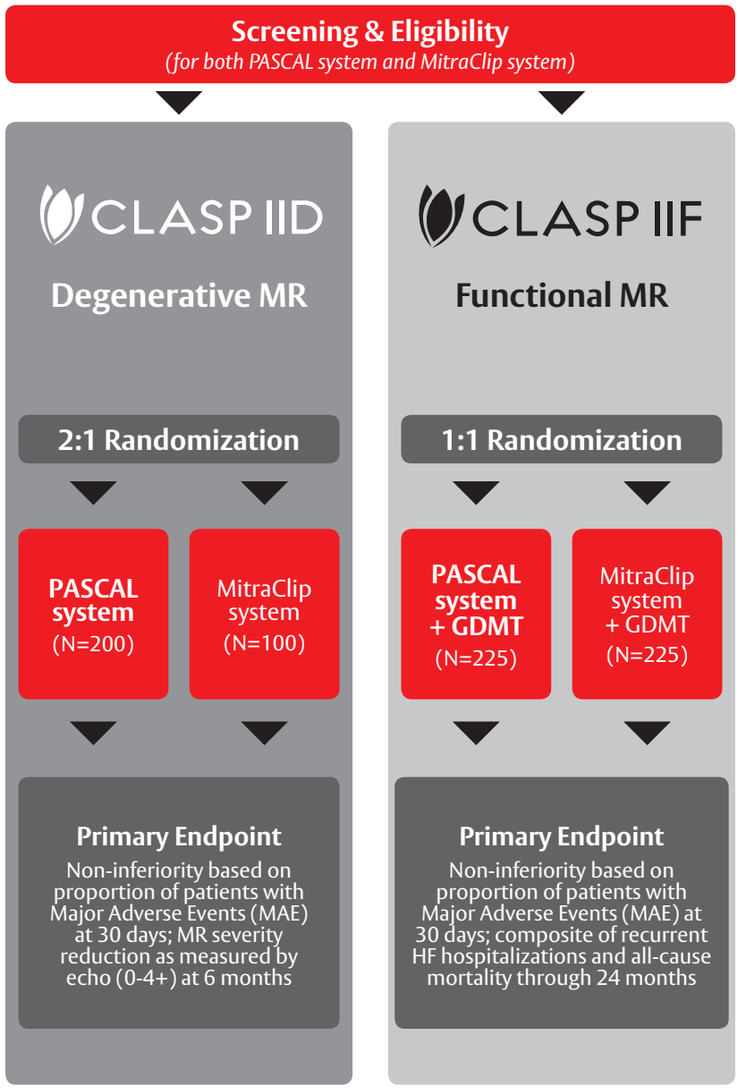

THE CLASP IID/IIF TRIAL

For more detailed information about the CLASP IID/IIF trial, please visit:

www.clinicaltrials.gov

Search: NCT03706833

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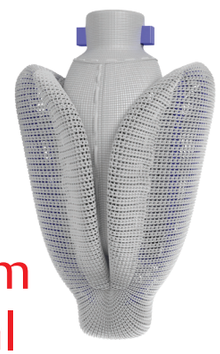
THE CLASP IID/IIF TRIAL

Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial



Trial Overview for Health Care Professionals

THE CLASP IID/IIF TRIAL

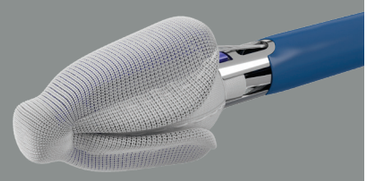
Trial Background & Objectives

Degenerative mitral valve regurgitation (DMR), also known as primary MR, refers to regurgitation resulting from structural abnormality of the mitral valve leaflets and/or valve apparatus. DMR is most commonly characterized by mitral valve prolapse due to myxomatous degeneration. Medical therapy has a limited role in the treatment of DMR as it fails to address the underlying pathology of mitral valve mechanical incompetence. Importantly, no medical treatment has been shown to be effective in preventing the consequences of volume overload in asymptomatic DMR and should not delay consideration of surgical intervention in patients with symptoms or evidence of left ventricular systolic dysfunction. When performed before left ventricular (LV) dysfunction has occurred, mitral repair maintains LV function and restores lifespan to normal when practiced in expert hands. Unfortunately, it is estimated that up to 50-70% of DMR patients do not receive surgical mitral valve repair or replacement.

Functional mitral regurgitation (FMR), also referred to as secondary MR, is driven by adverse left ventricular remodeling due to ischemic or non-ischemic myocardial disease. Current guidelines are reluctant to advise isolated valve surgery for FMR, as the prognostic benefit of surgical valve repair or replacement in typical heart failure patients is unclear. Optimized medical therapy is of limited efficacy in patients with significant FMR for the reduction of heart failure related morbidity and mortality. Despite the excess mortality associated with MR, a significant number of patients with MR are not referred to surgery as they may be considered inoperable or at high surgical risk because of age or comorbidities.

In cases of both DMR and FMR, there is an unmet need for alternative, catheter-based, minimally invasive approaches.

Product Under Clinical Investigation



PASCAL transcatheter valve repair system

Objective

The objective of this prospective, multicenter, randomized, controlled pivotal trial is to evaluate the safety and effectiveness of transcatheter mitral valve repair with the Edwards PASCAL Transcatheter Valve Repair System compared to Abbott MitraClip in patients with degenerative mitral regurgitation (DMR) who have been determined to be at prohibitive risk for mitral valve surgery by the Heart Team, and in patients with functional mitral regurgitation (FMR) on guideline directed medical therapy (GDMT).

Patients will be seen for follow-up visits at discharge, 30 days, 6 months, and annually through 5 years.

CLASP IID Cohort - Degenerative MR

- Transcatheter mitral valve repair in patients with degenerative mitral regurgitation with either Edwards PASCAL system or Abbott MitraClip

CLASP IIF Cohort - Functional MR

- Transcatheter mitral valve repair in patients with functional mitral regurgitation with either Edwards PASCAL system + GDMT or Abbott MitraClip + GDMT

Primary Endpoints

1. PASCAL system is not inferior to MitraClip with respect to the proportion of patients with major adverse events (MAE) at 30 days. The primary safety endpoint is a composite of MAEs.
2. PASCAL system is not inferior to Mitraclip with respect to the proportion of patients with MR severity reduction as measured by echocardiography using a scale of 0-4+ at 6 months.
3. PASCAL system is not inferior to MitraClip with respect to the proportion of patients with recurrentheart failure hospitalizations and all-cause mortality at 24 months.

Secondary Endpoints

1. Rates of various adverse events at 6 and 12 months.
2. Functional improvement as measured by an increase (in meters) in 6 minute walk test (6MWT) at 30 days, 6 months, and 1 year.
3. Functional improvement (quality of life) as measured by an increase (in points) in Kansas City Cardiomyopathy Questionnaire (KCCQ) at 30 days, 6 months, and 1 year.
4. Functional improvement (quality of life) as measured by an increase (in points) of Short Form Health Survey (SF-36) at 30 days, 6 months, and 1 year.

Key Inclusion Criteria

- Eighteen (18) years of age or older
- Patient is able and willing to give informed consent and follow protocol procedures, and comply with follow-up visit requirements
- Patient is determined to be at prohibitive risk for mitral valve surgery by the heart team (CLASP IID cohort only)
- Patient is on stable heart failure medications/Guideline Directed Medical Therapy (CLASP IIF cohort only)
- Patient is determined to be a candidate for transcatheter mitral valve repair by the heart team for both PASCAL system and MitraClip
- Mitral regurgitation (3+ to 4+) by echo
- Suitable valve and regurgitant jet morphology
- Elevated BNP > 150 pg/ml or corrected NT-pro BNP of > 600 pg/ml or heart failure hospitalization within the past 12 months (CLASP IIF cohort only)

Key Exclusion Criteria

- Patient in whom a TEE is contraindicated or screening TEE is unsuccessful
- Mitral valve anatomy which may preclude proper PASCAL system or MitraClip access, use and/or deployment or sufficient reduction in mitral regurgitation
- Patient with refractory heart failure requiring advanced intervention (i.e. biventricular pacemakers, left ventricular assist device, transplantation) (ACC/AHA Stage D heart failure)
- Clinically significant, untreated coronary artery disease
- Recent stroke
- Other severe valve disorders requiring intervention
- Need for emergent or urgent surgery for any reason or any planned cardiac surgery within the next 12 months
- Any prior mitral valve surgery (except surgical annuloplasty) or transcatheter mitral valve procedure
- Active rheumatic heart disease or rheumatic etiology for MR
- Severe aortic stenosis or regurgitation
- Known history of severe symptomatic carotid stenosis
- History of deep vein thrombosis (DVT) or pulmonary embolism (PE)
- Severe COPD
- Pregnant or planning pregnancy within next 12 months. Note: Female patients of childbearing potential need to have a negative pregnancy test performed within 14 days prior to intervention and be adherent to an accepted method of contraception
- Concurrent medical condition with a life expectancy of less than 12 months in the judgment of the Investigator
- Patient is currently participating in another investigational biologic, drug or device clinical study where the primary study endpoint was not reached at time of enrollment
- Other medical, social, or psychological conditions that preclude appropriate consent and follow-up, including patients under guardianship