



Cryoablation for Monomorphic Ventricular Tachycardia

Revision G

Protocol Number CS-098

(Eudamed No. CIV-20-07-034205)

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21 October 2022

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TITLE	Cryoablation for Monomorphic Ventricular Tachycardia (VT)
OBJECTIVE	The objective of this clinical study is to evaluate the safety and performance of the Adagio VT Cryoablation System in the ablation treatment of Monomorphic VT
INVESTIGATIONAL DEVICE	<p>The investigational device is the Adagio Medical VT Cryoablation System (Adagio System) that includes the following:</p> <ul style="list-style-type: none"> • The Cryoablation Console (P/N 109-0010-001 with VT software 106-1009-001 Rev.01) • The VT Cryoablation Catheter (P/N 109-0017-001)
INTENDED USE	The Adagio VT cryoablation system is intended to create transmural, linear and focal lesions to cardiac structures in the ventricles with cryoablation
PROPOSED INDICATION FOR USE	The Adagio Medical VT Cryoablation System is indicated for the treatment of monomorphic ventricular tachycardia by ablation of arrhythmogenic tissue that drives and maintains these arrhythmias.
STUDY DESIGN	<p>A prospective, single-arm, multi-center, pre-market, clinical study designed to provide safety and performance data regarding the use of the Adagio Medical VT Cryoablation System in the treatment of ventricular tachycardia.</p> <p>Study subjects will include patients who experience recurrent monomorphic VT and are scheduled for an endocardial VT ablation. Study subjects have or will have an Implantable Cardioverter Defibrillator (ICD) prior to hospital discharge following the cryoablation procedure.</p> <p>A VT ablation procedure is performed by finding the abnormal ventricular heart tissue that is causing the VT and applying energy with an ablation catheter to the area. The goal is to apply energy to create a scar or destroy the tissue that causes the VT, such that VT is no longer present or inducible.</p>
STUDY SIZE	Up to 60 subjects
INVESTIGATIONAL SITES	Up to 10 Clinical Sites
STUDY DURATION	The study is anticipated to take approximately 18 months to enroll and will include a 12-month follow-up period for each patient. Total study duration is anticipated to be about 30 months.
STUDY PRIMARY ENDPOINTS	<p><u>The Primary Endpoint for Safety</u> is an analysis of the proportion of subjects who are free from definite or probable device/procedure related <u>Major Adverse Events</u> (MAEs) that occur during or within 30 days following the cryoablation procedure. MAEs include any of the following:</p> <ul style="list-style-type: none"> • Death

	<ul style="list-style-type: none"> • Myocardial infarction • Cardiac perforation/pericardial tamponade • Cerebral infarct or systemic embolism • Major bleeding requiring transfusion • Mitral, Tricuspid or Aortic valve damage resulting in moderate or severe regurgitation • Access site complications requiring medical or surgical intervention • Pericarditis • Heart block requiring a permanent pacemaker • Other serious adverse device effects (SADEs), including TIAs, adjudicated by an independent DSMB to be probably or definitely related to the Adagio System. <p>The Primary Endpoint for Clinical Performance is an analysis of the proportion of patients receiving a single cryoablation procedure with freedom from ventricular tachycardia lasting longer than 30 seconds or appropriate ICD intervention until the end of the 6 month follow up period.</p> <p>The Primary Endpoint for Procedure Performance is an analysis of the proportion of subjects with non-inducible clinical monomorphic VT at the conclusion of the initial cryoablation procedure.</p>
STUDY SECONDARY ENDPOINTS	<p><u>Safety</u></p> <ul style="list-style-type: none"> • The proportion of study subjects with probable or definite device or procedure related serious adverse events (SAEs) including MAEs as described above, or serious adverse device effects (SADEs) between 30-days and up to 12 months post-procedure. Events will be adjudicated by an independent Data and Safety Monitoring Board (DSMB) for relatedness to the Adagio System. <p><u>Performance</u></p> <ul style="list-style-type: none"> • The proportion of study subjects with non-inducible sustained monomorphic VT at the end of the ablation procedure • The proportion of study subjects with freedom from Ventricular Tachycardia lasting longer than 30 seconds at 12 months without the use of anti-arrhythmic drugs (AADs) • The proportion of study subjects with freedom from Ventricular Tachycardia lasting longer than 30 seconds at 12 months with previously failed AADs • Reduction of VT burden at 6 and 12 months

	<p><u>Descriptive Statistics</u></p> <ul style="list-style-type: none"> • Procedure fluoroscopy time • Total ablation time • Total procedure time • Number and location of cryoablation lesions • Number of inducible clinical VTs before and after cryoablation • Number of appropriate and inappropriate ICD therapies (shocks and antitachycardia pacing, ATP) in the follow up period • Mapping and ablation strategies utilized during the ablation procedure • Freedom from cardiovascular (CV) hospitalizations or CV-related ER visits through 12 months • Recording of the use of AADs in the follow up period
STUDY POPULATION	<p>The patient population will consist of men and women ≥ 18 years of age and scheduled for an endocardial ablation of monomorphic VT (new onset VT and/or VT despite antiarrhythmic therapy). A potential study patient will be eligible for study enrollment only if all the following inclusion criteria apply:</p> <p><u>Inclusion Criteria (IC)</u></p> <p>IC 1 Male or female the ages of ≥ 18 years</p> <p>IC 2 Eligible for a catheter ablation due to Ischemic and/or non-ischemic recurrent symptomatic sustained monomorphic Ventricular Tachycardia also defined as having a similar QRS configuration from beat to beat.</p> <p>IC 3 Has or will be receiving an ICD prior to hospital discharge post procedure.</p> <p>IC 4 Refractory to at least one AAD (Refractory is defined as an AAD not able to treat the arrhythmia satisfactorily or induces unwanted side effects).</p> <p>IC 5 Subject has LVEF $> 20\%$, confirmed by echo or comparable technique in the previous 3 months or during baseline evaluation</p> <p>IC 6 Willingness, ability, and commitment to participate in baseline and follow-up evaluations for the full length of the study</p> <p>IC 7 Willingness and ability to give an informed consent</p> <p>A potential study patient will be eligible for study enrollment only if none of the following exclusion criteria applies:</p> <p><u>Exclusion Criteria (EC)</u></p>

	<p>EC 1 Any known objective contraindication to ventricular tachycardia ablation, TEE, or anticoagulation, including but not limited to the identification of any cardiac thrombus or evidence of sepsis</p> <p>EC 2 Any duration of continuous arrhythmia that is not monomorphic ventricular tachycardia. Multiple monomorphic tachycardia is acceptable, but polymorphic VT is not.</p> <p>EC 3 Any VT ablation within 4 weeks prior to enrollment</p> <p>EC 4 More than one prior (>4 weeks) Ventricular Tachycardia ablation or prior surgical treatment for ventricular tachycardia</p> <p>EC 5 Ventricular tachycardia secondary to electrolyte imbalance, active thyroid disease, or any other reversible or non-cardiac cause</p> <p>EC 6 Structural heart disease as described below:</p> <ul style="list-style-type: none"> a. Class IV heart failure b. Aortic aneurysm c. Previous cardiac surgery or percutaneous coronary intervention within 60 days prior to the procedure d. Interatrial baffle, closure device, patch, or PFO occlusion device e. IVC filter f. Coronary artery bypass graft (CABG) procedure within six (6) months prior to the ablation procedure g. Severe Mitral or Aortic insufficiency or stenosis based on most recent TTE h. Cardiac myxoma i. Significant congenital anomaly j. Recent Myocardial Infarct (MI) or unstable angina, within 60 days prior to the ablation procedure k. Mechanical aortic or mitral valve <p>EC 7 Any previous history of cryoglobulinemia</p> <p>EC 8 History of blood clotting or bleeding disease</p> <p>EC 9 Any prior history of documented cerebral vascular accident (CVA), TIA or systemic embolism (excluding a post-operative Deep Vein Thrombosis, DVT), within 6 months prior to the ablation procedure.</p> <p>EC 10 Breastfeeding, pregnant, or anticipated pregnancy during study follow-up</p> <p>EC 11 Current enrollment in any other study protocol where testing or results from that study may interfere with the procedure or outcome measurements for this study</p> <p>EC 12 Any other condition that, in the judgment of the investigator, makes the patient a poor candidate for this procedure, the study or compliance with the protocol (includes vulnerable</p>
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	patient population, mental illness, addictive disease, candidate for heart transplantation, patient with ventricular assist device, or terminal illness with a life expectancy less than 12 months)
FOLLOW UP	7-day (phone contact), 30-day, 3-month, 6-month, & 12-month
DATA COLLECTION	See Table Below