Cardiol Therapeutics

Impact of CardiolRx™ on Recurrent Pericarditis

ClinicalTrials.gov Identifier: NCT05494788

MAvERIC-Pilot is a Phase 2 multi-center, open-label, pilot study assessing the impact of CardiolRx™ (cannabidiol) oral solution, on recurrent pericarditis

Introduction

Managing recurrent pericarditis which is refractory or intolerant to current treatments is particularly challenging

- Current first- and second-line management consists of NSAIDs, colchicine and corticosteroids
- Chronic corticosteroid use has been associated with serious adverse effects and increased risk of recurrence
- Third-line therapy includes anakinra and rilonacept, both of which inhibit IL-1 activity
- Recurrences may also occur following discontinuation of these immunosuppressive biologics

IL-1 = Interleukin 1; NSAIDs = non-steroidal anti-inflammatory drugs

The Therapeutic Target

- Pericarditis is often triggered by a viral infection or pericardial insult, resulting in aberrant activation of the inflammasome signaling pathway
- NLRP3 inflammasome protein components are activated which induce the release of pro-inflammatory cytokines (e.g., IL-1α, IL-1β, IL-6, & IL-18), that:
  - Perpetuates endothelial dysfunction
  - Impairs vasodilation
  - Activates leukocytes
- This leads to pericardial damage, increased pericardial space and thickness, and a cyclic release of IL-1α

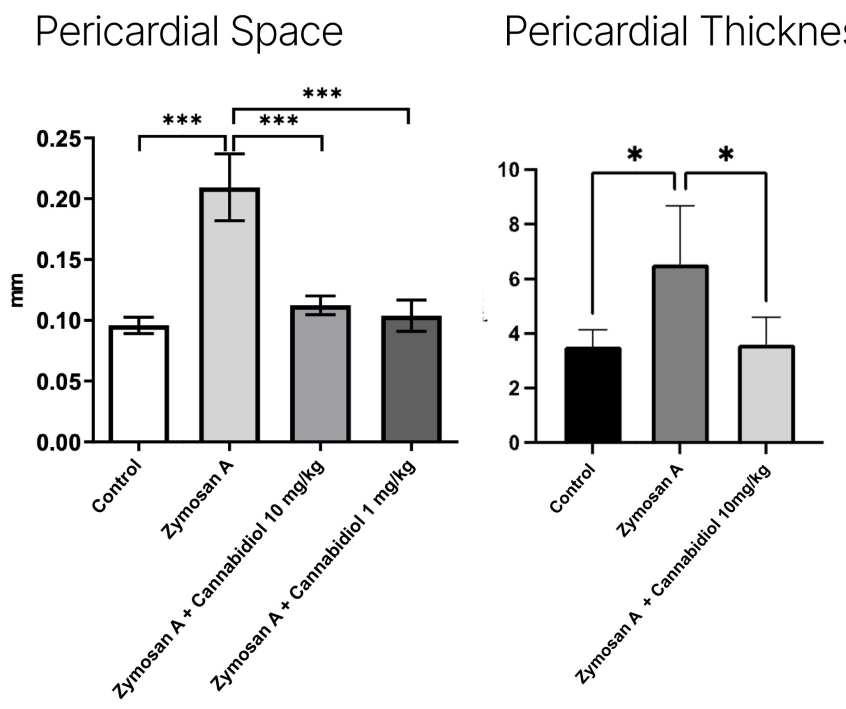
Targeting the upstream intracellular inflammasome signaling process represents a novel approach for the treatment of recurrent pericarditis

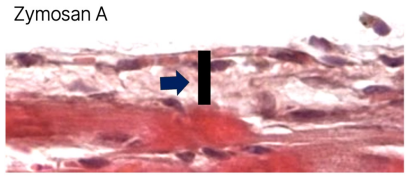
IL = Interleukin; NLRP3 = NACHT, leucine-rich repeat, and pyrin domain-containing protein 3

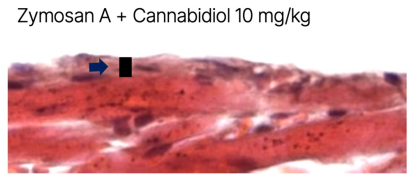
Study Intervention

- CardiolRx™ is a pharmaceutically manufactured synthetic cannabidiol solution, formulated for oral administration
- Research suggests that the drug substance in CardiolRx™ attenuates multiple inflammatory signaling pathways, including inhibiting activation of the NLRP3 inflammasome
  - Significantly reduced pericardial effusion and thickness in a murine model of acute pericarditis
  - Significantly decreased the pro-inflammatory cytokines IL-1β and IL-6 and inhibited pro-IL-1β and NLRP3 mRNA expression *in vitro*

IL = Interleukin; NLRP3 = NACHT, leucine-rich repeat, and pyrin domain-containing protein 3







MAvERIC-Pilot Study Objectives

Efficacy

The primary efficacy objective is to evaluate the effect of CardiolRx™ on patient-reported pericarditis pain score using an 11-point Numerical Rating Scale (NRS), following 8 weeks of treatment

The study will also assess the feasibility of weaning concomitant pericarditis treatments, including corticosteroids, while taking CardiolRx™

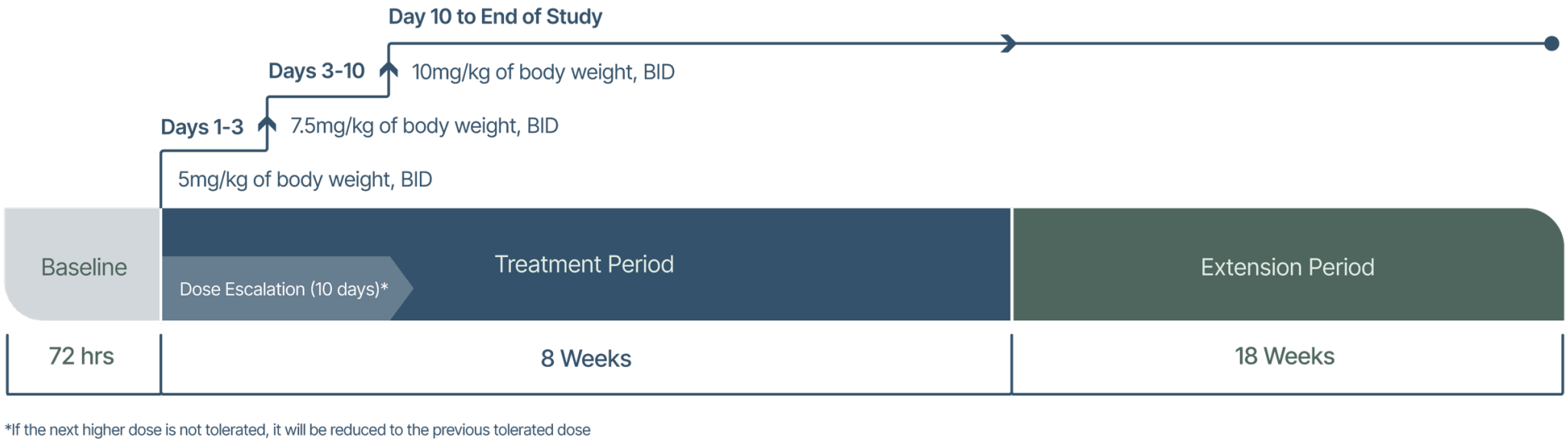
Safety

The primary safety objective is to demonstrate that administration of CardiolRx™ in the proposed doses in this patient population is safe, as determined by measuring several parameters

Study Design

- This is a Phase 2 multi-center, open-label, pilot study
- Participants will be enrolled in the study for approximately 26 weeks:
  - 72-hour Screening/Baseline Period
  - 8-week Treatment Period
  - 18-week Treatment Extension Period
- The dose of CardiolRx™ will be titrated from 5 mg/kg up to 10 mg/kg of body weight BID over the first 10 days of the Treatment Period
- 10 mg/kg BID (or the highest tolerated dose) will be taken for the duration of the study
- During the 18-week Extension Period concomitant medications for pericarditis will be weaned under careful supervision

Study Schema



*If the next higher dose is not tolerated, it will be reduced to the previous tolerated dose

Key Inclusion Criteria:

- Male or female patients aged ≥18 years
- Diagnosis of at least 2 episodes of recurrent pericarditis
- At least 1 day with pericarditis pain score ≥4 on the 11-point NRS within the prior 7 days
- CRP ≥1.0 mg/dL OR evidence of pericardial inflammation assessed by delayed pericardial hyperenhancement on cardiac MRI
- Currently receiving NSAIDs, colchicine or corticosteroids for treatment of pericarditis (in any combination) in stable doses

Additional eligibility criteria will be assessed by the study site team during screening

CRP, C-reactive protein; NRS, Numerical Rating Scale; NSAIDs, non-steroidal anti-inflammatory drugs; MRI, magnetic resonance imaging

Key Exclusion Criteria:

- Diagnosis of pericarditis secondary to the following etiologies:
  - Tuberculosis
  - Neoplastic, purulent or radiation etiology
  - Post-thoracic blunt trauma
  - Myocarditis
- Prior history of sustained ventricular arrhythmias or QT interval prolongation
- Taken any cannabinoid in the past month
- Current diagnosis of cancer (except for non-melanoma skin cancer)
- Immunosuppressive therapy with any of the following treatments:
  - Rilonacept
  - Anakinra
  - Canakinumab
  - Methotrexate
  - Azathioprine
  - Cyclosporine
  - Intravenous immune globulin (IVIG)

Additional eligibility criteria will be assessed by the study site team during screening

What are the potential benefits for participants?

- Participants' overall health and pericarditis symptoms will be closely monitored during the study
- The results of the study could increase the knowledge about the use of cannabidiol in recurrent pericarditis

What are the potential risks for participants?

- Risks associated with study procedures (e.g. risks of blood sampling, irritation due to ECG pads, etc.)
- Potential for hypersensitivity or allergic reaction to the study medicine
- Adverse reactions to the study medicine may include:
  - Diarrhea
  - Fatigue
  - Somnolence
  - Suicidal thoughts
  - Decreased appetite
  - Malaise
  - Skin rash
  - Sleep disorder/insomnia
  - Increased liver enzymes
  - Infections
- Risks associated with weaning concomitant treatments for recurrent pericarditis

Site Contacts and Referral Information

If you have patients under your care who may be eligible for this study, please consider them for referral to the participating sites listed below.

Pima Heart and Vascular Clinical Research

Tucson, Arizona, United States, 85719
Contact: Thomas Waggoner, DO
Email: tom.waggoner@pimaheart.com
Make a Referral | Pima Heart and Vascular

Virginia Commonwealth University Health

Richmond, Virginia, United States, 23298
Contact: Georgia Thomas, MD
Email: georgia.thomas@vcuhealth.org
Refer a Patient | VCU Health

University of Vermont Medical Center

Burlington, Vermont, United States, 05401
Contact: Tracy Hagerty, MD
Email: Tracy.Hagerty@uvmhealth.org
Refer a Patient (uvmhealth.org)

MedStar Health Research Institute

Washington, District of Columbia, United States, 20010
Contact: Syed Haider, MD
Email: syed.w.haider@medstar.net
Physician Referral | MedStar Health

Site Contacts and Referral Information (cont.)

Mayo Clinic

Rochester, Minnesota, United States, 55905

Contact: S. A. Luis, MD

Email: luis.s@mayo.edu

Principal Investigator: S. A. Luis, MD

Provider relations - Medical Professionals - Mayo Clinic

Cleveland Clinic

Cleveland, Ohio, United States, 44195

Contact: Sonya Mihalus, BSN

Email: MIHALUS@ccf.org

Medical Professionals: Refer a Heart Patient | Cleveland Clinic

Minneapolis Heart Institute Foundation

Minneapolis, Minnesota, United States, 55407

Contact: David Lin, MD

Email: David.Lin@allina.com

Referring patients | Allina Health Minneapolis Heart Institute | Allina Health