RETROSPECTIVE EXPERIENCE OF CIED IMPLANTATION WITH PIEDMONT ATHENS REGIONAL ELECTROPHYSIOLOGY

STUDY SPONSOR:
AZIYO BIOLOGICS, INC.
1100 OLD ELLIS ROAD, SUITE 1200
ROSWELL, GA 30076

PROTOCOL NUMBER:
CPR-2212C

NCT #04351269

Protocol Date:
December 2, 2020

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Investigator Statement of Compliance

I hereby agree to comply with this protocol and applicable regulations governing clinical trials, including local regulations, and Good Clinical Practice/ICH Guidelines.

Investigator Signature: _____

Date: _____

Summary of Changes from Previous Version

Affected Section(s)	Summary of Revisions Made	Rationale
Study Synopsis, Design	Changed enrollment limit to 700 subjects from 600.	The enrollment limit was increased to allow the site the ability to enroll all available subjects.
Section 2, Study Design & Methods	Changed enrollment limit to 700 subjects from 600.	The enrollment limit was increased to allow the site the ability to enroll all available subjects.

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STUDY COORDINATION

STUDY SPONSOR	**AZIYO BIOLOGICS, INC.** 1100 OLD ELLIS ROAD, SUITE 1200 ROSWELL, GA 30076
DATA COORDINATION CENTER	**AZIYO BIOLOGICS, INC.** 1100 OLD ELLIS ROAD, SUITE 1200 ROSWELL, GA 30076

Study Synopsis

COMPANY	Aziyo Biologics, Inc.
PROTOCOL NO.	CPR-2212
PRODUCT(S)	CanGaroo® Envelope and Tyrx™ Absorbable Antibacterial Envelope
PROTOCOL TITLE:	Retrospective Experience of CIED Implantation with Piedmont Athens Regional Electrophysiology
OBJECTIVE	The objective of this study is to retrospectively gather information on patients who underwent a CIED procedure with either a CanGaroo, Tyrx envelope, or no envelope.
DESIGN	A single center will retrospectively review up to 700 subjects who underwent implantation of a CIED with CanGaroo, Tyrx, or no envelope. All sets of subjects enrolled will also be examined for any follow-up visits and/or adverse events that occurred up to 12 months post-surgery.
STUDY POPULATION	Male or female patients who underwent a CIED implantation utilizing CanGaroo hydrated in saline, CanGaroo hydrated in Antibiotic, Tyrx, or no envelope.
ENDPOINTS	The endpoints will be defined as: 1. The incidence of major infection post procedure. 2. Any pocket related issues that prompted an office visit
CLINICAL PARAMETERS	The following clinical data will be collected • Demographic information • Risk factors for infection • Surgical procedure • Type of device implanted • Envelope soak solution used • Post procedure information on major infections as defined below • Post procedure information on pocket related issues • Post procedure information on hematoma
DURATION	Data will be collected for a minimum of one post-surgical visit after CIED implant for all groups. If more visits are available, data from those visits will be collected up to 12 months post-procedure.
CENTERS	Single center in the U.S.

1. Introduction and Rationale

This document is a protocol for a human research study. This study is to be conducted according to U.S. and international standards of Good Clinical Practice in accordance with applicable Federal regulations, International Conference on Harmonization guidelines, and institutional research policies and procedures.

Broader indications for the implant of cardiac implantable electronic devices (CIED) and population aging are the main reasons for the continuous increase in the use of pacemakers, implantable cardioverter-defibrillators, and devices for cardiac resynchronization therapy. The rate of infection is out of proportion to the increase in implantation rate. This is primarily due to the comorbidities in CIED patients, the greater complexity of the devices, and the increased duration of procedures.[1,2,3]

2. Study Design and Methods

Clinical records will be reviewed and data collected for up to 700 subjects who underwent implantation of a CIED. All sets of subjects will have data reviewed for any visits on or after March 27, 2017. No subject will be excluded from the study based on gender, racial, or ethnic origin. Patients will not be contacted and only de-identified data will be collected. A waiver of Informed Consent and HIPAA authorization will be requested from the IRB.

Each patient's medical records will be reviewed by the investigator or designated personnel for basic clinical data, including demographic information, risk factors for infection, information about the surgical procedure, type of device implanted, and post procedure information on infection, pocket related issues, and hematoma information will all be collected for each subject. Data will be collected retrospectively using Electronic Data Capture (Medrio).

CIED infections are defined as (1) superficial cellulitis in the region of the CIED pocket with wound dehiscence, erosion, or purulent drainage, (2) deep incisional or organ/space (generator pocket) surgical site infection that meets the Centers for Disease Control and Prevention criteria, independent from time of surgery, (3) persistent bacteremia, or (4) endocarditis.

Major CIED infections are defined as a CIED infection resulting in one or more of the following:

- CIED system removal
- Any invasive procedure (e.g., pocket opened) without system removal

- Treatment with antibiotic therapy if the subject is not a candidate for system removal and infection recurrence after completion of antibiotic therapy or evidence of deep infection with wound dehiscence, erosion, or purulent drainage
- Death

Any serious adverse event that requires a Medical Device Report will be reported by the Sponsor to the FDA in accordance with Sponsor's Medical Device Reporting SOP. The site should contact:

Stephanie Richardson
678-492-4712
srichardson@aziyo.com

A code will be used to protect patient confidentiality. The key to the code will be kept separate from the data.

2.1 Schedule of Assessments

	Pre-Procedure Screening Visit	**Procedure Visit**	**Follow-up Visits (up to 12 mo.)**	**Unscheduled Visit**
Inclusion Determination	X			
Baseline Demographics	X			
Medical History/Risk Factors	X			
Type of Device Implanted		X		
Envelope Soak Solution Used		X		
Procedure Details		X		
Documentation of Complications		X		
Post-Operative Events			X	X
Infection Information/Culture Results			X	X
Pocket Related Issues			X	X

3. Study Objectives

The objective of the study is to:
1. The objective of this study is to retrospectively gather information on patients who underwent a CIED procedure with either a CanGaroo, Tyrx envelope, or no envelope.

Endpoints

The endpoints are defined as:
1. The incidence of major post procedure infection (as defined above)
2. Any pocket related issues that prompted an office visit which include but are not limited to pain, swelling, redness, migration and/or hematoma

4. Risks and Benefits

4.1.Risks

As this is a retrospective study, there are no physical potential risks to research subjects. There may be risks associated with loss of privacy.

4.2. Benefits

As this is a retrospective study, there are no physical benefit to individual research subjects; however, society and physicians will benefit from the knowledge gained.

5. Data Analysis

Since this is a retrospective study, analyses will consist of tabulated data and descriptive statistics. Subject data listings and tabular and graphical presentations of the summary and statistical results will be provided. Additional quantitative and qualitative comparisons will be made between the groups of subjects, contemporary literature, and similar studies. Statistical comparisons between treatment groups (CanGaroo versus Tyrx versus no envelope) will be performed using Fisher's exact test or Chi-square tests for categorical variables. Continuous variables will be analyzed using ANOVA. A log rank test will be performed to compare the time to infection between the CanGaroo, Tyrx, and no envelope treatment groups at all of the follow-up visits.

6. Ethical Considerations

6.1. Code of Conduct

The Investigator will ensure that the clinical study is conducted in accordance with good clinical practice and all regulatory and institutional requirements, including those for subject privacy, informed consent, Institutional Review Board, or Ethics Committee approval, and record retention.

6.2. Institutional Review Board Approval and Oversight

This protocol, or any subsequent modifications, will be reviewed and approved by an Institutional Review Board. A Waiver of Informed Consent and HIPAA due to the retrospective nature of this study will be requested.

The confidentiality of the identity of subjects enrolled in the study and the information contained in their study records will be maintained. Any publication of any data collected as part of this trial will only use de-identified data, so that identification of any individual subject will not be possible.

The records will be made available as required for review by the FDA, or other applicable regulatory agency and a reviewing IRB; however to the extent possible, the subject's identity will not be disclosed.

A subject identification number will be used during data collection and the patient name, date of birth, medical record number and/or address will NOT appear anywhere.

7. Bibliography

1. Mond HG, Proclemer A. The 11th world survey of cardiac pacing and implantable cardioverter-defibrillators: calendar year 2009 – a World Society of Arrhythmia's project, Pacing Clin Electrophysiol 2011; 34:1013–27. DOI: 10.1111/j.1540 8159.2011.03150.x; PMID: 21707667.

2. Beck H, Boden WE, Patibandla S, et al. 50th anniversary of the first successful permanent pacemaker implantation in the United States: historical review and future directions. Am J Cardiol 2010; 106:810–8. PMID: 21391322.

3. Khaldoun G Tarakji, Christopher R Ellis, Pascal Defaye and Charles Kennergren Cardiac Implantable Electronic Device Infection in Patients at Risk, ARRHYTHMIA & ELECTROPHYSIOLOGY REVIEW 2016.