

REPEL-CV[®]

BIORESORBABLE ADHESION BARRIER

REDUCES ADHESIONS IN CARDIAC SURGERY

US PIVOTAL CLINICAL TRIAL RESULTS

REPEL-CV[®]

SyntheMed, Inc. has developed REPEL-CV to reduce the formation of post-operative adhesions following cardiac surgery. REPEL-CV is an easy to use, non-adherent, compliant, transparent, bioresorbable and biocompatible polymeric film comprising poly-lactic acid (PLA) and polyethylene glycol (PEG). These components have been used extensively in implantable, absorbable medical devices as well as in drug coatings and have an established safety profile. The European Regulatory Authorities granted a CE Mark for REPEL-CV on August 23, 2006.

US Pivotal Clinical Trial - Preliminary Results

REPEL-CV is regulated by the FDA as a class III medical device. The pivotal clinical trial is typically the last trial required for review and approval by the FDA. REPEL-CV was evaluated in a multicenter, controlled pivotal clinical trial involving 15 cardiac surgical centers in the United States. This document highlights the preliminary results, which were submitted to the FDA as a basis for gaining approval to commercialize REPEL-CV in the United States. The pivotal study was titled:

“A Comparative, Evaluator-Masked, Randomized, Parallel, Multicenter Study to Determine the Safety and Effectiveness of REPEL-CV[®] for Reducing Post-Operative Adhesions Following Pediatric Cardiothoracic Surgery”

Fifteen US centers participated in the trial; the centers were all prestigious teaching institutions with a particular focus in pediatric CV surgery. All patients were new born babies diagnosed with congenital heart defects requiring a series of staged open heart surgical procedures. The first procedure was performed shortly after birth and the second procedure was performed about 6 months later. Fifty percent of the patients were randomized to control, which was the standard surgical procedure, and 50% received REPEL-CV placed over the retrosternal surface of the heart before the sternum was closed. A total of 103 patients met the protocol criteria and were evaluated at the second surgical procedure. The extent of the retrosternal surface involved with adhesions and the severity of the adhesions were determined at the second procedure using a 4 grade scale with Grade 0 being no adhesions and Grade 3 being dense, vascular (severe) adhesions.



Severity of adhesions was graded as follows:

Grade 0 = No adhesions

Grade 1 = Mild Adhesions (filmy, non-cohesive adhesions requiring blunt dissection to separate the space between the epicardium and sternum)

Grade 2 = Moderate adhesions (filmy, non-cohesive adhesions requiring a combination of blunt and selective sharp dissection to separate the space between the epicardium and the sternum)

Grade 3 = Severe adhesions (dense, cohesive adhesions requiring extensive sharp dissection to separate the space between the epicardium and the sternum)

Results

The primary clinical endpoint in the pivotal clinical trial protocol was to demonstrate a significant reduction in the mean extent of the retrosternal surface of the heart involved with severe (Grade 3) adhesions among the REPEL-CV treated patients as compared to the control patients. Using the 4 grade scale, a doctor preferably other than the doctor who performed the first procedure, made a determination during the second procedure, of the percent of the surface area with no adhesions and the percent of the remaining area involved in the three degrees of adhesions: filmy, moderate and severe. Based on surgeon interviews, the severe adhesions are often described as “clinically-significant adhesions” because they are the most difficult and time consuming to deal with during the secondary procedure. The severe adhesions are dense fibrous bundles which often have their own blood supply which require the surgeon to carefully and slowly dissect through these bundles in an attempt to avoid damage to critical cardiac structures.

Summary

- Comparative, Evaluator-Masked, Randomized, Parallel, Multicenter Study
- 15 US cardiothoracic surgery centers
- 54 REPEL-CV treated patients
- 49 control patients
- 70% of REPEL-CV treated patients were completely free of severe adhesions

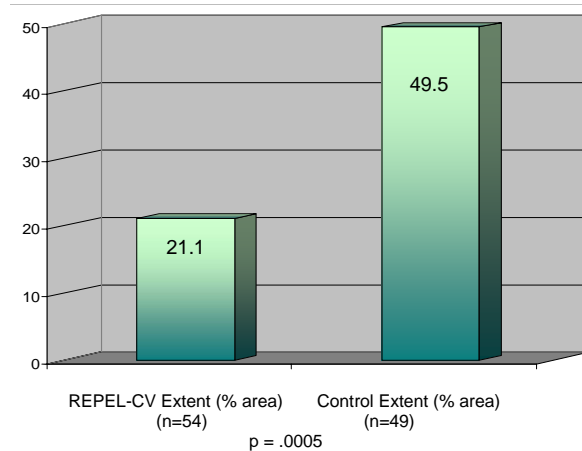
BENEFITS

- Less risk for the patient
- Less surgical time and anesthesia time
- Clearer plane of dissection for the surgeon
- Reduced cost for the hospital
- REPEL-CV significantly reduces retrosternal adhesions

Significant reduction in severe adhesions

The mean extent for the clinically-significant (severe) adhesions was calculated by adding up the percent of the surface area with Grade 3 adhesions for the 54 treated patients and for the 49 control patients and then dividing each of the totals by the number of patients in each group. For the 54 REPEL-CV treated patients, the mean extent was 21.1% of the retrosternal surface; whereas, for the control patients, the mean extent was 49.5% or 2.5 times greater. The p value (statistical significance) for this analysis was .0005. This significant reduction in clinically-significant adhesions should result in less risk for the patient, less surgical time and anesthesia time and a clear plane of dissection for the surgeon as well as reduced cost for the hospital. Graph 1 indicates the mean extent of clinically-significant (severe) adhesions for the REPEL-CV treated patients as compared to the control patients.

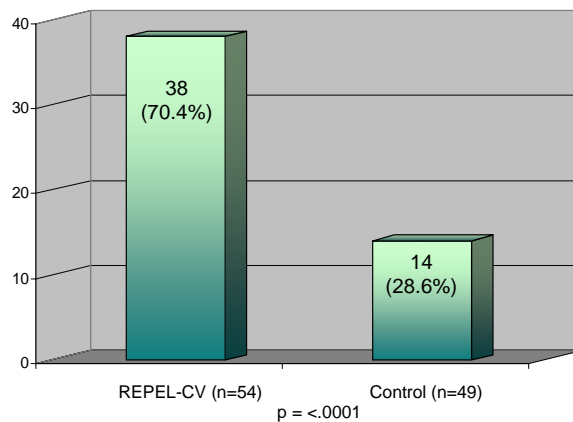
Graph 1: Mean Extent of Clinically-Significant (Severe) Adhesions



70.4% of REPEL-CV treated patients free of severe adhesions

Another key measure of the efficacy of REPEL-CV as measured in the pivotal clinical trial was the difference in the number of patients in the treated group who were completely free of clinically-significant (severe) adhesions as compared to the control group. Of the 54 per protocol patients treated with REPEL-CV, 38 patients or 70.4% of the patients were completely free of clinically-significant adhesions whereas only 14 control patients or 28.6% of the 49 control patients were free of clinically-significant adhesions. The p value was less than .0001. Graph 2 shows this comparison.

Graph 2: Patients (Percentage) with NO Clinically-Significant (Severe) Adhesions



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