SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Absorbable Hemostatic Agent

Device Trade Name: ETHIZIA Hemostatic Patch

Device Procode: SGV

Applicant's Name and Address: ETHICON, Inc.
1000 US Highway 202 South
Raritan, NJ 08869

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P240035/S002

Date of FDA Notice of Approval: June 25, 2026

The original PMA, P240035, was approved on December 15, 2025, and is indicated for: ETHIZIA Hemostatic Patch is indicated for use in adult patients with a body weight of ≥25kg as an adjunct to hemostasis in open liver surgery for minimal, mild, or moderate bleeding sites when control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.

The SSED to support the indication of ETHIZIA Hemostatic Patch (ETHIZIA) is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the device.

II. INDICATIONS FOR USE

ETHIZIA Hemostatic Patch is indicated for use in adult patients with a body weight of ≥25kg as an adjunct to hemostasis in open and minimally invasive surgical procedures on the liver for minimal, mild, or moderate bleeding sites when control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.

III. CONTRAINDICATIONS

- ETHIZIA is not indicated for use on severe (i.e., pulsatile) bleedings (defined by Surface Bleeding Severity Scale 4-5).
- ETHIZIA is not intended for intravascular use. Do not attempt to force ETHIZIA into blood vessels, and only apply ETHIZIA after standard surgical techniques have been used to close the vessel.
- ETHIZIA should not be used in infected wounds.
- ETHIZIA should not be used in patients with a known hypersensitivity to the component materials, including porcine proteins and FD&C Blue #1.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ETHIZIA Hemostatic Patch labeling.

V. DEVICE DESCRIPTION

ETHIZIA is a sterile, resorbable hemostatic patch that should be applied on a visible bleeding site. It is presented as a blue, soft, flexible, porcine gelatin (1 ± 0.2 grams per ETHIZIA) fiber-based gelatin carrier impregnated with NHS-POx / NU-POx granulate (1 ± 0.2 grams per ETHIZIA). Blue color (202 – 686 µg per ETHIZIA) is an aid to visualize ETHIZIA when applied onto a bleeding location. ETHIZIA measures 10 by 5 cm and can be applied on both sides. As ETHIZIA is a homogenously impregnated fibrous material, it is also suited to being torn into smaller pieces for application on irregularly shaped structures and areas that are difficult to access. Figure 1 shows a representative image of ETHIZIA. ETHIZIA product specifications are listed in Table 1.

The product is not removed at the end of surgery but is resorbed in 4-6 weeks.

Degradation of ETHIZIA depends upon several factors including the amount used, the anatomical location, and degree of saturation with blood or other fluids.



Figure 1. ETHIZIA

Table 1 – ETHIZIA Specifications	
Parameter	**Specification**
Appearance	Fibrous, coherent patch, homogeneously colored (blue)
Shape	Rectangular
Dimensions	Length: 100 ± 5 mm
	Width: 50 ± 5 mm
	Thickness: 5 ± 3 mm
Weight	1.6 – 2.5 g
Composition	Porcine gelatin (1 ± 0.2 grams per ETHIZIA)
	NHS POx/NU-POx granulate (1 ± 0.2 grams per ETHIZIA)
	FD&C Blue No. 1 (202 – 686 µg per ETHIZIA
Ratio Blue NHS-POx/NU-POx	Blue NHS-POx/NU-POx (75:25 (w/w) to 85:15 (w/w)
Loading (% of granulates in final finished device)	36-61%
Sterility assurance level (SAL)	10^{-6}

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of uncontrolled bleeding. Hemostasis involves the interaction of blood vessels, platelets, and the coagulation cascade to form a localized mechanical seal. A variety of adjunctive methods exist to achieve hemostasis. During a major hemorrhage, direct pressure or clamps may result in hemostasis. Minor bleeding can be controlled and stopped by ligation, pharmacological agents (topical thrombin and tissue sealants), laser cautery (heat, electric current, or a caustic substance) or topical agents such as oxidized cellulose, collagen, and gelatin sponges. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

ETHIZIA is CE Marked and was introduced into commercial distribution in Europe, the Middle East and Africa, and Asia in 2024, and the product is currently marketed in the countries listed in Table 2 below.

Table 2. CE-Marked Version of ETHIZIA Marketed Countries	
Europe	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Luxembourg, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, United Kingdom
Middle East and Africa	Bahrain, Israel, Jordan, Kuwait, Qatar, Saudi Arabia, United Arab Emirates
Asia	Hong Kong

In December 2024, Ethicon filed PMA P240035 and received FDA approval for ETHIZIA in December 2025.

The ETHIZIA Hemostatic Patch has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of adverse effects (e.g., complications) reported during clinical trials with ETHIZIA:

- Abdominal pain
- Abscess / Infection
- Application site hemorrhage (intra-operative bleeding / re-bleeding)
- Bile leak / biloma (post-operative)
- Hematoma
- Intra-abdominal fluid collection
- Pyrexia

Below is a list of potential adverse effects that may occur with the use of a product such as ETHIZIA:

- Allergic reaction
- Anemia
- Blockage of artery or vein/ischemia of organs
- Closing of intestinal tract
- Damage of organs and vessels
- External compression of tubular structures such as arteries, bile ducts, veins, bowel
- Gastrointestinal hemorrhage
- Haemobilia
- Hemostat migration, folding or fragmentation resulting in bowel erosion or obstruction
- Imaging artifact (resulting in unnecessary invasive diagnostic procedures or reoperation)
- Masking residual cancer at margin of resection resulting in higher local recurrence rates and decreased disease-free survival
- New surgery
- Pain
- Pseudo abscess
- Pseudo mass formation
- Pulsatile hematoma
- Rash
- Toxic response
- Thromboembolic event

IX. SUMMARY OF NON-CLINICAL STUDIES

Multiple non-clinical studies to support the safety and effectiveness of ETHIZIA, including design verification and validation, pre-clinical animal studies, biocompatibility, shelf life, packaging testing and sterilization, and endotoxin validation and testing were conducted. Please refer to the P240035 SSED available on the FDA website for a description of previously conducted studies.

Additional animal and usability studies were conducted to support the safety and effectiveness of ETHIZIA for its intended use in laparoscopic and robotic procedures and reported in Table 3 below.

Table 3. Summary of Non-Clinical Animal Studies

Study	Treatments Applied	Results
GLP hemostatic effectiveness trials		
Evaluation of the ETHIZIA laparoscopic application on bleeding sites in a swine model -Organ: liver -Lesion type: biopsy punch -Procedure type: laparoscopic	4 pigs 32 applications • 24 ETHIZIA • 8 Surgifoam + Thrombin (Topical RECOTHROM Thrombin (Baxter) was used in combination with every application of Surgifoam)	ETHIZIA achieved 96% hemostasis in 30 seconds, 100% in 5 minutes. Surgifoam + Thrombin 100% in 30 seconds. In 17% of the cases ETHIZIA needed a second patch and 0% a third patch. For Surgifoam + Thrombin 25% needed a second patch, and 13% a third patch.
Non-GLP studies		
Usability and performance of ETHIZIA on liver biopsy punch bleeding model in laparoscopic procedure -Organ: liver -Lesion type: biopsy punch -Procedure type: laparoscopic	2 pigs 16 bleeding sites 17 ETHIZIA pieces applied	Hemostasis was 81% (13/16) after initial 30 seconds of pressure, 94% (15/16) after 1 minute, and 100% at the primary endpoint of 3 minutes. No sites showed rebleeding within 30 minutes.

Table 3. Summary of Non-Clinical Animal Studies		
Study	**Treatments Applied**	**Results**
Usability and performance of ETHIZIA on large liver lesions in laparoscopic procedure[2] -Organ: liver, spleen -Lesion type: resection, metastasectomy, simulated traumatic lesion -Procedure type: laparoscopic	2 pigs 12 bleeding sites 25 ETHIZIA pieces applied TachoSil applied to 3 bleeding sites with 2 follow-up ETHIZIA rescue treatment	For ETHIZIA, hemostasis after 30 seconds was 78% (7/9) in the liver and 33% (1/3) in the spleen. All (100%) ETHIZIA sites were hemostatic at primary endpoint of 3 minutes. TachoSil (applied to sites with SBSS 3 or 4) failed to reach hemostasis in 3 minutes in all 3 sites, and ETHIZIA was applied as rescue treatment to 2 sites.
Usability performance of ETHIZIA on large liver lesions in robotic procedure[2] -Organ: liver, blood vessel -Lesion type: resection, metastasectomy -Procedure type: robotic	2 pigs 9 bleeding sites 17 ETHIZIA pieces applied TachoSil applied to 1 bleeding site with 1 follow-up ETHIZIA rescue treatment	For ETHIZIA, hemostasis of the liver was 86% (6/7) after the initial 30 seconds of pressure; the remaining liver site was hemostatic at 8 minutes. One blood vessel site with ETHIZIA was hemostatic after 30 seconds of pressure, the other at 3 min. The one TachoSil site was unsuccessful after 2 attempts in 10 minutes; ETHIZIA was applied for rescue treatment, with hemostasis after 30 seconds of pressure.
Comparison of ETHIZIA versus TachoSil on large liver lesions in robotic procedure -Organ: liver -Lesion type: superficial, resection, metastasectomy -Procedure type: robotic	4 pigs 18 bleeding sites 25 ETHIZIA pieces applied TachoSil applied to 18 bleeding sites with 1 follow-up ETHIZIA rescue treatment	For ETHIZIA, hemostasis was achieved in 83% (15/18) after 30 seconds of pressure and 100% after 5 minutes. Mean time to hemostasis was 64 ± 83 seconds. For TachoSil, hemostasis was 50% (9/18) at 5 minutes. Mean time to hemostasis was 220 ± 60 seconds (for those achieving hemostasis).

Table 3. Summary of Non-Clinical Animal Studies		
Study	**Treatments Applied**	**Results**
Comparison of ETHIZIA versus standard suturing during partial nephrectomy in robotic procedure[2] -Organ: kidney -Lesion type: resection -Procedure type: robotic	4 pigs 16 bleeding sites 37 ETHIZIA pieces Standard suturing applied to 16 bleeding sites	Compared to standard suturing, sites treated with ETHIZIA had significantly shorter procedure times, including warm ischemia (arterial clamping) time. Active bleeding during treatment application was found in 19% of ETHIZIA sites compared to 94% of suturing sites. For ETHIZIA, hemostasis was 81% (13/16) after 30 seconds of pressure, 88% (14/16) at 3 minutes, and 100% by 8 minutes. A relook at ~4 hours after initial hemostasis was achieved showed rebleeding in 0% of ETHIZIA sites compared to 12.5% of suturing sites.
ETHIZIA vs renorrhaphy in a robotic porcine partial nephrectomy survival model[2] -Organ: kidney -Lesion type: metastasectomy -Procedure type: robotic	12 pigs 18 ETHIZIA applications 18 standard suturing	ETHIZIA achieved hemostasis in 72% in 30 seconds, 78% in 2 minutes, 83% in 3 minutes, 88% in 6 minutes, 94% in 8 minutes and 100% in 9 minutes. ETHIZIA provided persistent hemostasis without signs of rebleeding over the course of a 6-week survival period. The primary use of ETHIZIA on a defect in the calyx was sufficient to provide adequate sealing over the course of tissue healing without the risk of urine leakage over a course of 6 weeks. No signs of migration of ETHIZIA, and degradation within 6 weeks.
[1]The performance of ETHIZIA™ in anticoagulated patients has not been studied. [2]The safety and effectiveness of ETHIZIA™ has not been established for use in anatomic locations other than the liver.		

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of ETHIZIA as an adjunct to hemostasis in minimally invasive surgical procedures on the liver for minimal, mild or moderate bleeding sites when control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical under IDE G230105 (NCT05900037). Data from this clinical study were the basis for the PMA approval decision.

G230105 is a prospective, randomized (1:1), multicenter, pivotal IDE clinical investigation for subjects undergoing elective minimally invasive liver or gallbladder resection surgery. With a total of 53 eligible subjects randomized to ETHIZIA (n=25) or SURGICEL Original (n=28) at 6 clinical sites in the US. A summary of the descriptive clinical study is presented below.

A. Study Design

Patients were treated between October 6, 2023 and April 25, 2025. The database for this Panel Track Supplement reflected data collected through August 2025 (database lock) and included 53 patients. There were 6 investigational sites.

This study was a pre-market, prospective, randomized, multicenter, pivotal clinical investigation evaluating the safety and effectiveness of ETHIZIA versus SURGICEL Original (Control) for hemostasis during minimally invasive liver and gallbladder surgery. The primary objective of this investigation was to evaluate minimally invasive use of ETHIZIA in robotic and laparoscopic liver and gallbladder surgery. In this investigation, hemostasis was defined as a grade of 0 (None/Dry) on the Surface Bleeding Severity Scale (SBSS).

The study was conducted in compliance with United States Food and Drug Administration (FDA) regulations 21 CFR Parts 50, 54, 56, and 812, and International Council for Harmonization (ICH) E6 Good Clinical Practices (GCP). Sponsor collaborated with a Contract Research Organization (CRO) for study management, data management, site activation, site monitoring and data verification, medical writing, Independent Data Monitoring Committee (IDMC) and Independent Adjudication Committee (IAC) facilitation.

An IDMC, comprised of independent medical experts and an expert biostatistician, oversaw the study throughout its duration to minimize bias through periodic review of blinded data pertaining to trial conduct, patient selection, and safety and effectiveness endpoints.

An IAC of independent physicians reviewed all serious adverse events (SAEs) and adverse events of special interest (AESI; i.e., bleeding-related events, thromboembolic events, biloma, and allergic reaction) occurring during the 3-month

follow-up after surgery for relatedness to the device and expectedness of the event based on the clinical scenario comprising of patient and procedural characteristics.

SURGICEL Original, an absorbable hemostat (oxidized regenerated cellulose), was used as the control. The clinical trial choice of comparator control product was based on the following considerations:

- The control is a legally marketed alternative with similar indications for use.
- A standard-of-care hemostatic patch to obtain the highest standards of clinical evidence when compared to the investigational device.
- Both products being ready-to-use, which limits blood loss during surgery and increases the comparability in safety and performance.
- Both products have similar risk-benefit ratio for patches because of position and structure of the patch on the target bleeding site in relation to the patient anatomy.
- SURGICEL Original has been used as a comparator in hepatobiliary procedures in over 400 trial subjects.

Subjects were randomized intraoperatively in a 1:1 ratio to ETHIZIA or SURGICEL Original. The pivotal minimally invasive surgery (MIS) study treated 53 subjects: 25 patients randomized to ETHIZIA and 28 patients randomized to SURGICEL Original. Subjects were treated between October 2023 and April 2025. There were 6 investigational sites enrolling patients. Subjects were blinded to their randomized treatment group. Due to the physical differences in the investigational and control devices, surgeons could not be blinded. To minimize investigator bias during this clinical investigation, a validated bleeding scale was used to assess the severity of bleeding before randomization and to evaluate hemostasis after patch use. Because the baseline bleeding severity was assessed prior to randomization the investigator was not aware of the treatment assignment when scoring the baseline bleeding site.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Study was limited to patients who met the following inclusion criteria:

- Subject is scheduled to undergo elective minimally invasive (robotic or laparoscopic) surgery on the liver, including cholecystectomy;
- Subject is willing and able to give written informed consent for the clinical investigation participation;
- Subject is 22 years of age or older at the time of enrollment; and
- Subject has been informed of the nature of the clinical investigation.

In addition, subjects must have met the following intraoperative inclusion criteria:

- Subject undergoes a fully minimally invasive surgical approach without the use of a hand port at the time of randomization and application of the patch;

- Subject in whom the Investigator can identify a target bleeding site at the liver resection plane or cholecystectomy liver bed for which any applicable conventional means for hemostasis (e.g. suture, ligature or cautery) are ineffective or impractical and the choice is made to use a hemostat agent to stop the bleeding; and
- Pressure on the surface of the hemostatic agent can be applied with the minimally invasive instruments to achieve hemostasis; and
- Subject has a target bleeding site with a Surface Bleeding Severity Score (SBSS) of 1, 2, or 3. (e.g., reflecting minimal, mild, or moderate bleeding severities).

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- The target bleeding site is from a large defect in an artery or vein that requires vascular reconstruction with maintenance of vessel patency;
- Subject is scheduled to undergo surgery on organs other than the liver and its associated biliary and vascular system, except for combined colorectal surgery;
- Subject is scheduled to undergo a staged liver surgery procedure (e.g., Associating Liver Partition and Portal vein ligation for Staged hepatectomy [ALPPS])
- Subject is taking multiple antithrombotic therapies in therapeutic dosage up to the time of surgery, but allowing exclusive use of acetylsalicylic acid;
- Subject has platelet count <100 x 109/L, an activated partial thrombin time of >100s, or international normalized ratio >2.5;
- Subject has a total bilirubin level of ≥2.5 mg/dl;
- Subject is pregnant, planning on becoming pregnant or actively breastfeeding during the 3-month follow-up period;
- Subject has a known hypersensitivity to brilliant blue (FD&C Blue #1), or porcine gelatin;
- Subject who has religious objections to receiving products containing porcine;
- Subject has an active or suspected infection at the bleeding site;
- Subject in whom the investigational device will be used at the site of a synthetic graft or patch implant;
- Subject has a life expectancy of less than 3 months;
- Subject has a documented severe congenital or acquired immunodeficiency;
- Subject has had or has planned to receive any organ transplantation;
- Subject is currently participating or has participated in another clinical investigation within the past 30 days that may affect the endpoints of the study, such as trials related to the surgical procedure and anti-coagulation;
- Subject is not appropriate for inclusion in the clinical investigation, per the medical opinion of the Investigator; and

- Subject has any incidental (pre- and peri-operative) findings deemed by the Investigator to potentially jeopardize the safety or welfare of the subject.

2. Follow-up Schedule

All subjects were scheduled to return for a follow-up visit at week 6 (± 2 weeks), which included a laboratory and ultrasound imaging assessment. An onsite or telephone assessment took place at week 12 (± 2 weeks). Adverse events and complications were recorded at all visits as well as relevant concomitant medications. Study procedures are summarized in Table 4, and the patient laboratory test schedule is summarized in Table 5 below.

Preoperatively, information was collected on baseline demographics (age, sex, race and ethnicity), medical history (allergies, smoking status, cardiac disorders, systemic hypertension, renal dysfunction, diabetes, hereditary blood disorders, blood transfusions in the last 3 months, previous abdominal surgery, liver disease, portal hypertension, malignancies and prior therapies, indication for surgery, other critical medical condition or previous surgery, and American Society of Anesthesiologists classification), physical examination, relevant concomitant medications, and laboratory test data. Inclusion/exclusion criteria were confirmed preoperatively as well as intra-operatively.

Postoperatively, the objective parameters measured during the study included hemostatic performance data (including primary and secondary study endpoints), surgical procedural data (type of MIS, device handling, surgery date, procedure length, number of devices used, blood loss in ml, SBSS of target bleeding site, use of adjunct hemostatic agents/techniques, pneumoperitoneum, amount of material needed, user satisfaction (ETHIZIA only, per investigator, per procedure), hospitalization information (duration of stay in intensive care unit, total hospitalization period, blood transfusions), intra- and post-operative adverse events, device deficiencies, and laboratory test data. At the week 6 visit the study procedure included imaging of the resection, laboratory tests, collection of adverse events and relevant (new) concomitant medications. The week 12 visit could either be conducted onsite or via phone call and included collection of adverse events and relevant (new) concomitant medications.

Table 4. Schedule of Assessments					
Assessments	**Screening/ Baseline (< 6 Weeks Before Surgery)**	**Treatment**	**Post-Surgery to Hospital Discharge**	**Week 6 (±2 Weeks)**	**Week 12 (±2 Weeks)**
Informed consent	X				
Inclusion and exclusion criteria	X	X			
Baseline demographics and medical history (including allergies)	X				
Medication (including those impacting coagulation)	X		X	X	X
Physical examination	X		X	X	
Laboratory tests	X		X	X	
Procedural data (including primary efficacy endpoint and Device Deficiency)		X			
User satisfaction questionnaire		X			
Adverse Event assessments (with specific attention to bleeding and thrombotic events)		X	X	X	X

Table 5. Laboratory Testing Schedule			
Laboratory Tests	**Screening/ Baseline[a]**	**Through Admission[b]**	**Week 6 (±2 Weeks)**
Hematology			
Complete blood count	X	X	X
Coagulation			
Prothrombin time	X	X	[b]
Activated partial thromboplastin time	X	X	[b]
INR	X	X	[b]
Chemistry			
Bilirubin	X	X[c]	X
Calcium	X	[b]	[b]
Potassium	X	[b]	[b]
Sodium	X	[b]	[b]
Chloride	X	[b]	[b]
Albumin	X	X	X
Creatinine	X	X	[b]
AST	X	X	X
ALT	X	X	X
Gamma glutamyl transferase	X	X	X
Other			
Pregnancy test (if applicable)	X	N/A	N/A

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; N/A, not applicable.

a. Laboratory tests had to be performed at least once before surgery during the screening/baseline visit, with the latest data being the final presurgical data used in analyses.

b. Only collected as per standard of care hospital routine.

c. Including drainage fluid of the surgical drain, if applicable.

The key timepoints and assessments are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to efficacy, the primary performance endpoint is defined as delivery and adherence of the agent to the target bleeding site and achievement of hemostasis (defined by a grade of 0 on the SBSS, within 7 minutes from introduction of the first (piece of) patch through the trocar without rebleeding at the 10-minute timepoint from initiating pressure on the entire surface of the hemostatic agent and without the need to convert the surgical approach or use a hand port due to issues with hemostasis at the target bleeding site or device use. Hemostasis was defined as grade of 0

(None/Dry) on the SBSS, of the direct surface onto which ETHIZIA or Control was applied. The combination of the first target bleeding site and any other bleeding sites treated with the hemostatic device were referred to as all target bleeding sites. Results for hemostasis across all treated target bleeding sites are summarized in Tables 15 and 16.

No formal hypotheses are specified for this study. All study endpoints were summarized descriptively.

The estimated sample size was 50 subjects, with 25 subjects undergoing treatment with ETHIZIA as assigned by 1:1 randomization.

The primary analysis for the primary endpoint was performed using modified intent-to-treat (mITT), and supportive analysis was performed using the per-protocol (PP) population. The key secondary endpoint analysis was performed using the mITT population.

Secondary efficacy endpoints of this clinical investigation consisted of:

- Median time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis (seconds);
- Median time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the agent (seconds);
- Median time to hemostasis from initiating pressure on the entire surface of the agent (seconds);
- Percentage of hemostasis from initiating pressure on the entire surface of the agent at 30, 60, 120, 180, 240, 300, 360, 420, 480, 540 and 600 seconds;
- Kaplan-Meier estimated distribution of time to hemostasis from initiating pressure on the entire surface of the agent;
- Treatment failure, defined as no hemostasis with the agent at 10 minutes from initiating pressure on the entire surface of the agent;
- Rebleeding after the 10-minute time point from initiating pressure on the entire surface of the agent but before subject wound closure; and
- Number of times an additional (piece of) hemostatic agent needs to be used to achieve hemostasis.

With regards to safety, the incidence, severity and relation to hemostatic device of all AEs were assessed. The AEs for the ETHIZIA group were compared to those for the Control group. All AEs were collected, with AEs of special interest being:

- Bleeding-related events, including rebleeding of the bleeding site(s) treated with hemostatic patch at any point in time (within 10 minutes of application, prior to subject closure, and postoperative), and including hematoma;
- Thromboembolic events;
- Biloma; and
- Allergic reaction.

The following exploratory endpoints were collected:

- Conversion from minimally invasive to open surgery, and reasons for conversion;
- Procedure duration (minutes);
- Duration of hepatic blood inflow reduction (minutes);
- Estimated blood loss (mL) during surgery;
- Number and type of blood transfusions during hospitalization;
- Duration of Intensive Care Unit (ICU) stay;
- Total hospitalization time;
- Postoperative drainage volume, characteristics, and duration;
- Need for and cause of reoperation;
- Imaging of the liver resection at 6 weeks post-surgery to detect (1) fluid collection and its size (in mL) and aspect, (2) pseudo-aneurysm, (3) encapsulation of the agent, and (4) rolling up of the agent on the resection plane;
- Amount of hemostatic material needed; and
- User satisfaction (questionnaire) for ETHIZIA.

4. Statistical Analysis Plan

No formal hypotheses were specified for this trial. All trial endpoints were summarized descriptively. For descriptive purposes, the 95% CI was provided for the primary efficacy endpoint and the key secondary efficacy endpoint (i.e., median time from introducing the first [piece of] hemostatic agent through the trocar and achieving hemostasis [seconds]).

Continuous variables were summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables were summarized using frequencies and percentages of subjects in each category.

5. Sample Size

The planned sample size was 50 subjects, with 25 subjects undergoing treatment with ETHIZIA as assigned by 1:1 randomization. A minimum of 50% of the subjects were planned to be enrolled in the US to help ensure that the subjects were representative of the US population for which this device was to be indicated. This sample size was chosen to reflect a focus on the usability of ETHIZIA during a MIS, where the aim was to provide descriptive data on the specific features of minimally invasive use, while a powered safety and efficacy assessment of ETHIZIA was being evaluated in a pivotal IDE trial (G210325).

6. Analysis Set Definitions

The All-Enrolled Population included all subjects who signed the informed consent form (ICF). The All-Enrolled Population was used for subject disposition and screen failure summaries.

The Safety Population included all randomized subjects who received treatment with ETHIZIA or SURGICEL Original. The treatment group assignment in the Safety Population was defined by the treatment actually received. The Safety Population was used for the analysis of safety endpoints.

The mITT Population included all randomized subjects who did not have i) a change in SBSS to ineligible (SBSS of 0, 4, or 5) between randomization and treatment; and ii) death of a subject between randomization and treatment. The treatment group assignment was designated according to initial randomization. The mITT Population served as the basis for the analysis of all efficacy endpoints.

The Per-Protocol (PP) population included all subjects in mITT Population who received treatment with ETHIZIA or SURGICEL Original as randomized, had an assessment of the primary efficacy endpoint, and had no major CIP deviations impacting the primary efficacy endpoint.

7. Interim Analysis

A descriptive interim analysis of primary efficacy endpoint and AE data was performed to support the regulatory review of the open IDE clinical trial when approximately 50% of the subjects were randomized. The data required for the interim analysis were source data verified. The database did not undergo a formal database lock. No changes were made to the trial conduct based on this interim analysis.

B. Accountability of PMA Cohort

At the time of the database lock, a total of 94 subjects signed informed consent and were enrolled in the PMA study. 40 subjects were screen-failed, and 54 patients were randomized to receive either ETHIZIA (N=26) or SURGICEL Original (N=28). One subject in the ETHIZIA treatment arm met the withdrawal criteria (change in SBSS to 0) after randomization and was therefore not treated with the product or followed up for the trial. Of the 25 ETHIZIA patients who received treatment, 21 completed the trial and 4 withdrew or were lost to follow-up. In the SURGICEL Original treatment arm 28 patients received the treatment and completed the trial; there were no withdrawals or lost to follow-up subjects. There were no deaths in either treatment arms. Subject disposition after randomization is highlighted in Table 6.

Table 6. Subject Disposition of randomized subjects			
Category	**ETHIZIA (N=26) n (%)**	**SURGICEL Original (N=28) n (%)**	**Overall (N=54) n (%)**
Subjects randomized	26 (100)	28 (100)	54 (100)
Subjects treated	25 (96.2)[a]	28 (100)	53 (98.1)
Subjects completed the trial (up to 12-week follow-up visit)	21 (80.8)	28 (100)	49 (90.7)
Subjects who withdrew from the trial prematurely	5 (19.2)	0	5 (9.3)
Withdrawal of consent	0	0	0
Investigator's and sponsor's decision	0	0	0
Procedural eligibility criteria were not met	1 (3.8)[a]	0	0
Non-compliance to protocol	0	0	0
Lost to follow-up	2 (7.7)	0	2 (3.7)
Adverse event	0	0	0
Death	0	0	0
Other	2 (7.7)[b]	0	2 (3.7)

Abbreviations: N, number of subjects in the population; n, number of subjects with the specified outcome;

a. One subject in the ETHIZIA treatment group was withdrawn from the trial due to an exclusionary SBSS result between randomization and the planned application of the ETHIZIA Patch (SBSS changed to 0).

b. Two subjects in the ETHIZIA treatment group were not seen on site by the trial team at the 12-week follow-up visit, but the subjects' electronic health records were observationally followed by the site through 12 week study period to evaluate for AEs.

Note: Percentages were based on the number of randomized subjects in each group.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population were typical for liver surgery performed in the US. Subject demographics and operative characteristics are summarized below in Table 7. The mean age of subjects treated with ETHIZIA was 59.6 ± 14.4 years and the mean age of subjects treated with SURGICEL Original was 54.7 ± 14.2 years. The indications for surgery for subjects treated with ETHIZIA were hepatic cyst(s) (20.0%), cholangiocarcinoma (12.0%), cholecystitis or gall stones (12.0%), colorectal metastases (12.0%), hepatocellular carcinoma (12.0%), non-colorectal metastases (12.0%) and other (16.0%; metastatic leiomyosarcoma of the liver (4.0%), pneumobolia and contracted gallbladder (4.0%), adenocarcinoma (4.0%) and metastatic (to liver) cutaneous malignant melanoma (4.0%). The indications for surgery for subjects treated with SURGICEL

Original were benign tumor (17.9%), cholecystitis or gall stones (17.9%), hepatocellular carcinoma (17.9%), cholangiocarcinoma (14.3%), colorectal metastases (14.3%), hepatic cyst(s) (7.1%), and other (7.1%; Hurthle cell carcinoma (3.6%) and hepatic mass concerning hepatocellular carcinoma (3.6%)). Type of resections were similar between both groups for anatomic and non-anatomic resections – 68.0% of ETHIZIA surgeries were non-anatomic, and 67.9% of SURGICEL Original subjects underwent non-anatomic resections. Majority of minimally invasive surgeries across both groups were robotic (ETHIZIA: 68.0% and SURGICEL Original: 71.4%).

Table 7. Subject Demographic and Operative Characteristics (Safety Population)

	ETHIZIA (n=25)	**SURGICEL Original (n=28)**
Age (years)		
Mean (SD)	59.6 (14.39)	54.7 (14.24)
Median	60.0	52.5
Min, Max	32, 80	24, 79
Sex, n (%)		
Male	13 (52.0)	14 (50.0)
Female	12 (48.0)	14 (50.0)
Race, n (%)		
White	18 (72.0)	20 (71.4)
Asian	1 (4.0)	3 (10.7)
Black or African American	1 (4.0)	2 (7.1)
Other	5 (20.0)	3 (10.7)
Ethnicity, n (%)		
Hispanic or Latino	5 (20.0)	5 (17.9)
Not Hispanic or Latino	19 (76.0)	23 (82.1)
Other	1 (4.0)	0
Child Pugh classification, n (%)		
A	13 (52.0)	14 (50.0)
B	0	0
C	0	0
N/A	12 (48.0)	14 (50.0)
ASA classification, n (%)		
1	0	1 (3.6)
2	4 (16.0)	6 (21.4)
3	20 (80.0)	21 (75.0)
4	1 (4.0)	0
5	0	0
Indication for surgery, n (%)		
Benign tumor	1 (4.0)	5 (17.9)
Cholangiocarcinoma	3 (12.0)	4 (14.3)
Cholecystitis or gall stones	3 (12.0)	5 (17.9)
Colorectal metastases	3 (12.0)	4 (14.3)
Hepatocellular carcinoma	3 (12.0)	5 (17.9)

Table 7. Subject Demographic and Operative Characteristics (Safety Population)		
	ETHIZIA (n=25)	**SURGICEL Original (n=28)**
Non colorectal metastases	3 (12.0)	0
Hepatic cyst(s)	5 (20.0)	3 (10.7)
Other[a]	4 (16.0)	2 (7.1)
Minimally Invasive Surgery, n (%)		
Robotic	17 (68.0)	20 (71.4)
Laparoscopic	8 (32.0)	8 (28.6)
Procedure Duration (minutes)		
Mean (SD)	164.7 (80.80)	170.9 (106.01)
Median (range)	169.0 (52, 352)	137.0 (54, 452)
Type of resection, n (%)		
Anatomic	7 (28.0)	6 (21.4)
Non-anatomic	17 (68.0)	19 (67.9)
N/A	1 (4.0)	3 (10.7)
Extent of resection, n (%)		
Cholecystectomy	4 (16.0)	5 (17.9)
Left hemihepatectomy	2 (8.0)	2 (7.1)
Right hemihepatectomy	1 (4.0)	2 (7.1)
Extended left hemihepatectomy	0	0
Extended right hemihepatectomy	0	0
Segmentectomy	8 (32.0)	7 (25.0)
Bisegmentectomy	7 (28.0)	4 (14.3)
Trisegmentectomy	0	0
Non-anatomical wedge resection	3 (12.0)	7 (25.0)
Missing	0	1 (3.6)
Vascular reconstruction performed, n (%)	0	1 (3.6)
Biliary tree reconstruction performed, n (%)	0	0
Visible bile leakage surgically treated during surgery, n (%)	0	1 (3.6)
Estimated total size of resection (cm^2), Mean ± SD	85.8 ± 82.6	82.1 ± 83.3
Estimated mean (SD) blood loss (mL)	270.8 (433.20)	226.4 (502.27)
Median (range) blood loss (mL)	100 (5 – 2000)	50 (2 – 2600)
Blood transfusion during surgery (any), n (%)	2 (8.0)	1 (3.6)
Red blood cells	0	0
Plasma	0	0
Other		
Blood transfusion post-surgery (any), n (%)	2 (8.0)	1 (3.6)

Table 7. Subject Demographic and Operative Characteristics (Safety Population)		
	ETHIZIA (n=25)	**SURGICEL Original (n=28)**

Abbreviations: BMI, body mass index; Max, maximum; Min, minimum; mL, milliliter; N, number of subjects in the Safety Population; n, number of subjects with available data in each category; SD, standard deviation.

Notes: Percentages were based on the total of each categorical variable. Age is in years and is the age of the subject at the time of randomization; height was measured at the screening/baseline visit; weight was measured at admission before surgery.

[a.] The other indications of surgery were metastatic hurthle cell carcinoma, metastatic leiomyosarcoma of the liver, pneumobolia and contracted gallbladder, adenocarcinoma, metastatic (to liver) cutaneous malignant melanoma', and hepatic mass concerning for HCC-cancer.

Target bleeding site information is summarized Table 8 below. The majority of the first target bleeding sites bleeding surface type were either flat surface (ETHIZIA: N=13, 52.0%; SURGICEL Original: N=12, 42.9%) or irregular surface (ETHIZIA: N=11, 44.0%; SURGICEL Original: N=13, 46.4%). Only a few first target bleeding sites had a bleeding surface type being dimple or pit (ETHIZIA: N=1, 4.0%, SURGICEL Original N=3, 10.7%). The mean target bleeding site size for the first target bleeding site in the ETHIZIA treatment group was 6.2 cm^2 and for SURGICEL Original treatment group 5.4 cm^2. Both the ETHIZIA treatment group and SURGICEL Original treatment group first target bleeding sites had more venous bleeding (ETHIZIA: N=17, 68.0%; SURGICEL Original: N=17, 60.7%), followed by mixed (ETHIZIA: N=7, 28.0%, SURGICEL Original: N=9, 32.1%) and arterial (ETHIZIA: N=1, 4.0%, SURGICEL Original: N=2, 7.1%). The ETHIZIA treatment group had more first target bleeding sites with an SBSS 3 (N=9, 36.0%) compared to the SURGICEL Original Treatment group (N=6, 21.4%), while the SURGICEL Original Treatment group had more SBSS 1 (N=12, 42.9%) compared to the ETHIZIA treatment group (N=8, 32.0%). Use of primary hemostatic techniques prior to applying patch and assessing SBSS were done in 48.0% of the first target bleeding sites in the ETHIZIA treatment group and in 57.1% of the SURGICEL Original treatment group.

As the Clinical Investigation Plan (CIP) allowed for multiple bleeding sites to be treated with the randomized product; an additional 10 bleeding sites were treated with ETHIZIA (N=35), and 1 additional bleeding site was treated with SURGICEL Original (N=29). For all treated target bleeding sites, bleeding site parameters for all target bleeding sites were generally similar to the first target bleeding site.

Table 8. Bleeding Site Information (Safety Population)			
First Target Bleeding site			
	Description	**ETHIZIA (N=25)**	**SURGICEL Original (N=28)**
Estimated total transected parenchyma area of current bleeding surface, maximum width (cm)	n	25	27
	Mean (SD)	8.876 (6.7257)	8.529 (5.5023)
	Median	8.00	7.00
	Min, Max	1.00, 35.00	1.00, 19.50
Estimated total transected parenchyma area of current bleeding surface, maximum length (cm)	n	25	27
	Mean (SD)	7.18 (3.689)	7.55 (5.294)
	Median	7.00	6.00
	Min, Max	1.0, 14.2	0.6, 21.0
Estimated size of total transected parenchyma area of current bleeding site, width × length (cm^2)	n	25	27
	Mean (SD)	63.576 (44.6792)	80.370 (84.4169)
	Median	50.00	48.00
	Min, Max	1.00, 151.94	1.00, 285.00
Target Bleeding site, n (%)	Flat Surface	13 (52.0)	12 (42.9)
	Irregular surface	11 (44.0)	13 (46.4)
	Dimple or pit	1 (4.0)	3 (10.7)
Estimated size of target bleeding site, width × length (cm^2)	Mean (SD)	6.20 (7.7889)	5.437 (4.5879)
	Median	4.0	4.0
	Min, Max	1.00, 30.00	0.24, 18.00
Bleeding type, n (%)	Arterial	1 (4.0)	2 (7.1)
	Venous	17 (68.0)	17 (60.7)
	Mixed	7 (28.0)	9 (32.1)
SBSS, n (%)	1	8 (32.0)	12 (42.9)
	2	8 (32.0)	10 (35.7)
	3	9 (36.0)	6 (21.4)
Use of primary hemostatic techniques	Yes	12 (48.0)	16 (57.1)
	Cautery	8 (32.0)	12 (42.9)
	Clips	1 (4.0)	0
	Staples	0	0
	Sutures/Ligatures	2 (8.0)	1 (3.6)
	Other	1 (4.0)	3 (10.7)
	No	13 (52.0)	12 (42.9)
Pneumoperitoneum level (mmHg), n (%)	≤ 9	0	0
	10	3 (12.0)	1 (3.6)
	11	1 (4.0)	2 (7.1)
	12	4 (16.0)	9 (32.1)
	13	1 (4.0)	3 (10.7)
	14	9 (36.0)	8 (28.6)
	15	7 (28.0)	5 (17.9)

Table 8. Bleeding Site Information (Safety Population)

Abbreviations: cm, centimeter; Max, maximum; Min, minimum; mmHg, millimeters of mercury; N, number of subjects in the Safety Population; n, number of subjects with available data in each category; SBSS, Surface Bleeding Severity Scale; SD, standard deviation.

Note: The presented frequencies and the denominator used to calculate percentages were based on subjects in each group in the Safety Population.

Surgical Procedure

The type of MIS was more frequently robotic (ETHIZIA treatment group: 68.0%; SURGICEL Original treatment group: 71.4%) compared to laparoscopic (ETHIZIA treatment group: 32.0%; SURGICEL Original treatment group: 28.6%). Three subjects in the SURGICEL Original treatment group (10.7%) and no subjects in the ETHIZIA treatment group required conversion to open surgery or the addition of a hand port. Of the conversions, none were related to the use of the product. The most common trocar size used for patch introduction was 12 mm (ETHIZIA treatment group: 96.0%; SURGICEL Original treatment group: 92.9%).

Washout periods were observed prior to surgery for acetylsalicylic acid, antiplatelet therapy, anticoagulation medications, and IV heparin, as no subjects in either treatment group were using these antithrombotic medications at the time of surgery. Similarly, no subjects were receiving oral Coumadin within 2 days before surgery. Only 1 subject from the SURGICEL Original treatment group was receiving antiplatelet medication within 5 days prior to surgery.

The extent of liver resection was balanced across the treatment groups, with the majority of subjects undergoing minor liver resection (segmentectomy, bisegmentectomy, non-anatomical wedge resection, and cholecystectomy); however, there was a notable difference (≥ 10%) between the treatment groups in the frequency of bisegmentectomies (ETHIZIA treatment group: 28.0%; SURGICEL Original treatment group: 14.3%) and non-anatomical wedge resections (ETHIZIA treatment group: 12.0%; SURGICEL Original treatment group: 25.0%). Non-anatomic resection was more common across both treatment groups (ETHIZIA treatment group: 68.0%; SURGICEL Original treatment group: 67.9%) compared to anatomic resection. The mean estimated total size of all resected areas was similar across the treatment groups (ETHIZIA treatment group: 85.8 cm2; SURGICEL Original treatment group: 82.1 cm2). One subject in the SURGICEL Original treatment group required vascular reconstruction. No subjects had biliary tree reconstruction. Visible bile leakage that was surgically treated was also infrequent in both treatment groups; only 1 subject in the SURGICEL Original treatment group required surgical treatment of a bile leak.

The most common type of resection method was vessel sealing system (ETHIZIA treatment group: 40.0%; SURGICEL Original treatment group: 32.1%), followed by the ‘other’ resection category (ETHIZIA treatment group: 40.0%; SURGICEL Original treatment group: 25.0%), which represents a combination of the methods

listed in Table 9; this table also includes the data of other possible resection methods used. Most subjects were not treated with a hepatic blood inflow reduction method (ETHIZIA treatment group: 72.0%; SURGICEL Original treatment group: 75.0%); for the remainder, the Pringle maneuver was the hepatic blood inflow reduction method used (ETHIZIA treatment group: 28.0%; SURGICEL Original treatment group: 25.0%), with a mean duration of which was shorter in the SURGICEL Original treatment group (ETHIZIA treatment group: 38.1 minutes; SURGICEL Original treatment group: 27.9 minutes).

The most frequent type of hepatic parenchyma was normal (ETHIZIA treatment group: 76.0%; SURGICEL Original treatment group: 67.9%), followed by steatotic hepatic parenchyma, which was more frequent in the SURGICEL Original treatment group (17.9%) compared to the ETHIZIA treatment group (12.0%).

The mean estimated blood loss during the procedures was similar across the treatment groups (ETHIZIA treatment group: 270.8 mL; SURGICEL Original treatment group: 226.4 mL). The numbers of subjects requiring intraoperative blood transfusions were similar across the treatment groups (2 subjects in the ETHIZIA treatment group versus 1 subject in the SURGICEL Original treatment group). All subjects had pneumoperitoneum reduced to 0 mm Hg for a period of at least 5 minutes, before the finalization of surgery. Surgical drains were used in 39.6% of all subjects without a meaningful difference between the treatment groups (ETHIZIA treatment group: 36%; SURGICEL Original treatment group 42.9%).

Table 9. Surgical Procedure Data (Safety Population

Category	**Response/ Description**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**	**Overall (N = 53)**
Type of MIS, n (%)	Total	25	28	53
	Laparoscopic	8 (32.0)	8 (28.6)	16 (30.2)
	Robotic	17 (68.0)	20 (71.4)	37 (69.8)
Need to convert to open surgery or add hand port, n (%)	Total	25	28	53
	Yes	0	3 (10.7)	3 (5.7)
	No	24 (96.0)	25 (89.3)	49 (92.5)
	Missing	1 (4.0)	0	1 (1.9)
Trocar size used for patch introduction, n (%)	Total	25	28	53
	12 mm	24 (96.0)	26 (92.9)	50 (94.3)
	15 mm	1 (4.0)	2 (7.1)	3 (5.7)
	Other	0	0	0
Subject was receiving acetylsalicylic acid up to time of surgery, n (%)	Total	25	28	53
	Yes	0	0	0
	No	25 (100)	28 (100)	53 (100)
Subject was receiving any other antiplatelet therapy up to time of surgery, n (%)	Total	25	28	53
	Yes	0	0	0
	No	25 (100)	28 (100)	53 (100)
	Total	25	28	53

Table 9. Surgical Procedure Data (Safety Population				
Category	**Response/ Description**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**	**Overall (N = 53)**
Subject was receiving anticoagulation up to time of surgery, n (%)	Yes	0	0	0
	No	25 (100)	28 (100)	53 (100)
IV heparin within 12 hours before surgery, n (%)	Total	25	28	53
	Yes	0	0	0
	No	25 (100)	28 (100)	53 (100)
Oral Coumadin within 2 days before surgery, n (%)	Total	25	28	53
	Yes	0	0	0
	No	25 (100)	28 (100)	53 (100)
Antiplatelet medications within 5 days prior to surgery, n (%)	Total	25	28	53
	Yes	0	1 (3.6)	1 (1.9)
	No	25 (100)	27 (96.4)	52 (98.1)
Extent of resection, n (%)	Total	25	28	53
	Cholecystectomy	4 (16.0)	5 (17.9)	9 (17.0)
	Left hemihepatectomy	2 (8.0)	2 (7.1)	4 (7.5)
	Right hemihepatectomy	1 (4.0)	2 (7.1)	3 (5.7)
	Extended left hemihepatectomy	0	0	0
	Extended right hemihepatectomy	0	0	0
	Segmentectomy	8 (32.0)	7 (25.0)	15 (28.3)
	Bisegmentectomy	7 (28.0)	4 (14.3)	11 (20.8)
	Trisegmentectomy	0	0	0
	Non-anatomical wedge resection	3 (12.0)	7 (25.0)	10 (18.9)
	Missing	0	1 (3.6)	1 (1.9)
Anatomic and non-anatomic resection, n (%)	Total	25	28	53
	Anatomic	7 (28.0)	6 (21.4)	13 (24.5)
	Non-anatomic	17 (68.0)	19 (67.9)	36 (67.9)
	N/A	1 (4.0)	3 (10.7)	4 (7.5)
Estimated total size of all resection areas (cm^2)	n	25	27	52
	Mean (SD)	85.8 (82.64)	82.1 (83.31)	83.9 (82.20)
	Median	70.0	50.0	57.0
	Min, Max	1, 325	1, 285	1, 325
Vascular reconstruction performed, n (%)	Total	25	28	53
	Yes	0	1 (3.6)	1 (1.9)
	No	25 (100)	27 (96.4)	52 (98.1)
Biliary tree reconstruction performed, n (%)	Total	25	28	53
	Yes	0	0	0
	No	25 (100)	28 (100)	53 (100)

Table 9. Surgical Procedure Data (Safety Population				
Category	**Response/ Description**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**	**Overall (N = 53)**
Visible bile leakage that was surgically treated, n (%)	Total	25	28	53
	Yes	0	1 (3.6)	1 (1.9)
	No	25 (100)	27 (96.4)	52 (98.1)
Resection method, n (%)	Total	25	28	53
	CUSA	1 (4.0)	1 (3.6)	2 (3.8)
	Harmonic scalpel	2 (8.0)	4 (14.3)	6 (11.3)
	Vessel sealing system	10 (40.0)	9 (32.1)	19 (35.8)
	Bipolar cauterizing scissors	2 (8.0)	5 (17.9)	7 (13.2)
	Non-cauterizing scissors	0	2 (7.1)	2 (3.8)
	Other	10 (40.0)	7 (25.0)	17 (32.1)
Blood inflow reduction method, n (%)	Total	25	28	53
	None	18 (72.0)	21 (75.0)	39 (73.6)
	Pringle maneuver	7 (28.0)	7 (25.0)	14 (26.4)
	Total vascular exclusion	0	0	0
	Other	0	0	0
Duration of blood inflow reduction (min)	n	7	7	14
	Mean (SD)	38.1 (20.89)	27.9 (14.36)	33.0 (18.03)
	Median	30.0	25.0	29.5
	Min, Max	25, 84	15, 55	15, 84
Type of hepatic parenchyma, n (%)	Total	25	28	53
	Normal	19 (76.0)	19 (67.9)	38 (71.7)
	Cirrhotic	2 (8.0)	3 (10.7)	5 (9.4)
	Steatotic	3 (12.0)	5 (17.9)	8 (15.1)
	Other	1 (4.0)	0	1 (1.9)
	Missing	0	1 (3.6)	1 (1.9)
Estimated blood loss during procedure (mL)	n	25	28	53
	Mean (SD)	270.8 (433.20)	226.4 (502.27)	247.4 (467.01)
	Median	100.0	50.0	100.0
	Min, Max	5, 2000	5, 2600	5, 2600
Intraoperative blood transfusion, n (%)	Total	25	28	53
	Yes	2 (8.0)	1 (3.6)	3 (5.7)
	No	23 (92.0)	27 (96.4)	50 (94.3)
Type of transfusion, n (%)	Total	2	1	3
	Red blood cells	2 (100)	1 (100)	3 (100)
	Platelets	0	0	0
	Plasma	0	0	0
	N/A	0	0	0

Table 9. Surgical Procedure Data (Safety Population				
Category	**Response/ Description**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**	**Overall (N = 53)**
Units of red blood cell transfusion	n	2	1	3
	Mean (SD)	1.5 (0.71)	2.0 (N/A)	1.7 (0.58)
	Median	1.5	2.0	2.0
	Min, Max	1, 2	2, 2	1, 2
Reason for transfusion, n (%)	Total	2	1	3
	Preoperative low Hb	0	0	0
	Intraoperative blood loss	2 (100)	1 (100)	3 (100)
	Combination of reasons	0	0	0
	Other	0	0	0
	N/A	0	0	0
Any additional transfusion, n (%)	Total	2	1	3
	Yes	0	0	0
	No	2 (100)	1 (100)	3 (100)
Patch applied, n (%)	Total	25	28	53
	Yes	25 (100)	28 (100)	53 (100)
Segments of the resection surface the patch was applied, n (%)	Total	25	28	53
	2	3 (12.0)	2 (7.1)	5 (9.4)
	2, 3	1 (4.0)	1 (3.6)	2 (3.8)
	2, 4	0	1 (3.6)	1 (1.9)
	3	0	2 (7.1)	2 (3.8)
	4	0	2 (7.1)	2 (3.8)
	4B	0	1 (3.6)	1 (1.9)
	4B, 7	1 (4.0)	0	1 (1.9)
	4a	0	1 (3.6)	1 (1.9)
	4b	2 (8.0)	4 (14.3)	6 (11.3)
	5	1 (4.0)	1 (3.6)	2 (3.8)
	6	2 (8.0)	0	2 (3.8)
	7	4 (16.0)	0	4 (7.5)
	8	0	1 (3.6)	1 (1.9)
	Bed of the gallbladder in lap cholecystectomy	1 (4.0)	0	1 (1.9)
	Cut Surface of segment 5/6	1 (4.0)	0	1 (1.9)
	Cut surface of Segments 5 and 7	1 (4.0)	0	1 (1.9)
	Cut surface of liver remnant	0	2 (7.1)	2 (3.8)
	Cut surface of segment 3	1 (4.0)	0	1 (1.9)
	Cut surface of segment 7	0	1 (3.6)	1 (1.9)
	Cut surface of segments 5 & 8	0	1 (3.6)	1 (1.9)

Table 9. Surgical Procedure Data (Safety Population				
Category	**Response/ Description**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**	**Overall (N = 53)**
	Deep resection margin	1 (4.0)	0	1 (1.9)
	Gallbladder bed	0	1 (3.6)	1 (1.9)
	Gallbladder fossa	2 (8.0)	0	2 (3.8)
	IV and V	0	1 (3.6)	1 (1.9)
	Left Lateral Segment 2	1 (4.0)	0	1 (1.9)
	Segment 4B	1 (4.0)	1 (3.6)	2 (3.8)
	Segment 5	1 (4.0)	1 (3.6)	2 (3.8)
	Segment 6	1 (4.0)	1 (3.6)	2 (3.8)
	Segment 8	0	1 (3.6)	1 (1.9)
	V	0	1 (3.6)	1 (1.9)
	VI	0	1 (3.6)	1 (1.9)
Segments of the resection surface the additional patches were applied, n (%)	Total	8	0	8
	4B, 7	1 (12.5)	0	1 (12.5)
	4b	1 (12.5)	0	1 (12.5)
	7	2 (25.0)	0	2 (25.0)
	All placed on segment 5	1 (12.5)	0	1 (12.5)
	Cut segments of 5 and 7	1 (12.5)	0	1 (12.5)
	Cut surface of segment 5/6	1 (12.5)	0	1 (12.5)
	Deep resection margin	1 (12.5)	0	1 (12.5)
Was pneumoperitoneum reduced to 0 mmHg for a period of at least 5 minutes, before finalization of surgery, n (%)	Total	25	28	53
	Yes	25 (100)	28 (100)	53 (100)
	No	0	0	0
Use of surgical drains, n (%)	Total	25	28	53
	Yes	9 (36.0)	12 (42.9)	21 (39.6)
	No	16 (64.0)	16 (57.1)	32 (60.4)
Occurrence of any surgical complications impacting postoperative outcomes, or AEs, during surgery, n (%)	Total	25	28	53
	Yes	0	2 (7.1)	2 (3.8)
	No	25 (100)	26 (92.9)	51 (96.2)

Abbreviations: AE, adverse event; CUSA, Cavitron Ultrasonic Surgical Aspirator; Hb, hemoglobin; IV, intravenous; Max, maximum; Min, minimum; MIS, minimally invasive surgery; mL milliliter; mmHG, millimeters of mercury; N, number of subjects in the Safety Population; n, number of subjects with available data in each category; N/A, not applicable; SD, standard deviation.

Note: Percentages were based on the total of each categorical variable.

Device Handling

Device handling is summarized in Table 10 for the Safety Population.

Across both treatment groups, most subjects had 1 piece of patch introduced through the trocar for the first target bleeding site (ETHIZIA treatment group 76%; SURGICEL Original 92.9%). Two pieces of patch were introduced through the trocar for the remainder of first target bleeding sites for each subject; no subjects had ≥ 3 pieces of patch introduced through the trocar to treat the subjects' first target bleeding sites. In the ETHIZIA treatment group, the majority of patches introduced through the trocar for the first target bleeding site across all subjects were cut into half sized pieces, followed by patches that were full sized and patches that were cut into to one-third– or one-fourth–sized pieces; in the SURGICEL Original treatment group, the majority of patches introduced through the trocar for the first target bleeding site across all subjects in this treatment group were patches that were full sized, followed by patches that were cut into half sized pieces and patches that were cut into one-third– or one fourth–sized pieces. Across both treatment groups, all of these (pieces of) patches were successfully introduced through the trocar to the subjects' first target bleeding sites (ETHIZIA treatment group: 31 pieces of patch across all 25 subjects' first target bleeding sites; SURGICEL Original treatment group: 30 pieces of patch across all 28 subjects' first target bleeding sites). In the ETHIZIA treatment group, after successful trocar introduction, 1 piece of patch was not successfully maneuvered to a subject's first target bleeding site and thus could not successfully be positioned on the bleeding site where sufficient pressure could be applied to control the bleed; however, the remaining 30 pieces of patch were successfully maneuvered and successfully positioned, and sufficient pressure was applied. In the SURGICEL Original treatment group, all 30 pieces of patch were successfully maneuvered and successfully positioned, and sufficient pressure was applied to the subjects' first target bleeding sites.

Device handling data for all target bleeding sites was generally similar to the first target bleeding site.

Table 10. Device Handling (Safety Population)			
		ETHIZIA (N = 25) n (%)	**SURGICEL Original (N = 28) n (%)**
Number of First Target Bleeding Sites	**n**	**25**	**28**
Number of pieces of patch that were introduced through the trocar for the first target bleeding site for each subject[a]	1	19 (76.0)	26 (92.9)
	2	6 (24.0)	2 (7.1)
	≥ 3	0	0
Total number of pieces of patch introduced through the trocar for the first target bleeding site across all subjects[b]	n	31	30
Proportion of patch introduced through the trocar[c]	1/4	2 (6.5)	3 (10.0)
	1/3	2 (6.5)	4 (13.3)
	1/2	15 (48.4)	6 (20.0)
	1	12 (38.7)	17 (56.7)
	Other	0	0
Piece of patch was successfully introduced[c]	Yes	31 (100)	30 (100)
	No	0	0
Piece of patch was successfully maneuvered to the target bleeding site[c]	Yes	30 (96.8)	30 (100)
	No	1 (3.2)	0
Piece of patch was successfully positioned on the bleeding site[c]	Yes	30 (96.8)	30 (100)
	No	1 (3.2)	0
Sufficient pressure was provided on the entire surface of the piece of patch with minimally invasive tools[c]	Yes	30 (96.8)	30 (100)
	No	1 (3.2)	0
Number of All Target Bleeding Sites	**n**	**35**	**29**
Number of pieces of patch that were introduced through the trocar for all target bleeding sites for each subject[d]	1	27 (77.1)	27 (93.1)
	2	8 (22.9)	2 (6.9)
	≥ 3	0	0
Total number of pieces of patch introduced through the trocar for all target bleeding sites across all subjects[b]	n	43	31
Proportion of patch introduced through the trocar[c]	1/4	6 (14.0)	3 (9.7)
	1/3	4 (9.3)	5 (16.1)
	1/2	20 (46.5)	6 (19.4)
	1	12 (27.9)	17 (54.8)
	Other (3×5 cm)	1 (2.3)	0

Table 10. Device Handling (Safety Population)			
		ETHIZIA (N = 25) n (%)	**SURGICEL Original (N = 28) n (%)**
Piece of patch was successfully introduced[c]	Yes	43 (100)	31 (100)
	No	0	0
Piece of patch was successfully maneuvered to the target bleeding site[c]	Yes	40 (93.0)	31 (100)
	No	3 (7.0)	0
Piece of patch was successfully positioned on the bleeding site[c]	Yes	39 (90.7)	31 (100)
	No	4 (9.3)	0
Sufficient pressure was provided on the entire surface of the piece of patch with minimally invasive tools[c]	Yes	39 (90.7)	31 (100)
	No	4 (9.3)	0

Abbreviations: N, number of subjects in the Safety Population; n, number of subjects/bleeding sites with available data in each category.

a. Percentages were based on the number of first target bleeding sites.
b. The total number of pieces of patch introduced was the sum of all pieces of patch across all subjects.
c. Percentages were based on the total number of pieces of patch introduced through the trocar.
d. Percentages were based on the number of all target bleeding sites.

Notes: Subjects may have had multiple patches used within the same group.

D. Safety and Effectiveness Results

1. Safety

The analysis of safety was based on all randomized subjects who received treatment with ETHIZIA (25) and SURGICEL Original (28). The key safety outcomes for this study are presented below in Tables 11 to 12. Adverse effects are reported in Table 13.

Overall, 30 (56.6%) subjects experienced at least 1 AE (73 events) as reported in Table 11 below. The percentage of subjects with at least 1 AE was 60.0% in the ETHIZIA treatment group (34 events in 15 subjects) and 53.6% in the SURGICEL Original treatment group (39 events in 15 subjects).

Overall, 5 (9.4%) subjects experienced at least 1 device-related AE per investigator assessment (i.e., ADE) (5 events). The percentage of subjects with device-related AEs per investigator assessment was 4.0% in the ETHIZIA treatment group (1 event in 1 subject) and 14.3% in the SURGICEL Original treatment group (4 events in 4 subjects).

Adverse Events related to device application were defined as AEs associated with the application of the device (but not the device itself or other procedures of the surgery). Overall, 2 (3.8%) subjects experienced at least 1 device application-related AE per

investigator assessment (2 events). The percentage of subjects with device application-related AEs per investigator assessment was 4.0% in the ETHIZIA treatment group (1 event in 1 subject) and 3.6% in the SURGICEL Original treatment group (1 event in 1 subject).

Overall, 6 (11.3%) subjects experienced at least 1 SAE (10 events). The percentage of subjects with SAEs was 16.0% in the ETHIZIA treatment group (5 events in 4 subjects) and 7.1% in the SURGICEL Original treatment group (5 events in 2 subjects). No subjects experienced SAEs that were considered device-related per investigator assessment (i.e., SADEs).

The percentage of subjects with AEs leading to device removal was 4.0% in the ETHIZIA treatment group where (1 event in 1 subject) and 14.3% in the SURGICEL Original treatment group (4 events in 4 subjects). All AEs leading to device removal had a preferred term (PT) of application site haemorrhage.

Device deficiencies were uncommon, affecting 1 (4.0%) subject in the ETHIZIA treatment group where it was reported that the patches (2 pieces of patch from 1 patch in total) became too soiled with blood prior to placement at the second target bleeding site (for usability of the patch). There was no device deficiencies reported for the SURGICEL Original treatment group.

Table 11. Overall Summary of Adverse Events (Safety Population)

Category	ETHIZIA (N = 25) n (%) e	SURGICEL Original (N = 28) n (%) e	Overall (N = 53) n (%) e
At least 1 AE	15 (60.0) 34	15 (53.6) 39	30 (56.6) 73
At least 1 SAE	4 (16.0) 5	2 (7.1) 5	6 (11.3) 10
At least 1 device-related AE per investigator assessment	1 (4.0) 1	4 (14.3) 4	5 (9.4) 5
At least 1 device application-related AE per investigator assessment	1 (4.0) 1	1 (3.6) 1	2 (3.8) 2
At least 1 AE leading to device removal	1 (4.0) 1	4 (14.3) 4	5 (9.4) 5
At least 1 AE leading to death	0	0	0
At least 1 AESI	5 (20.0) 7	5 (17.9) 7	10 (18.9) 14

Abbreviations: AE, adverse event; AESI, adverse event of special interest; e, number of events; N, number of subjects in the Safety Population; n, number of subjects with data available in each category; SAE, serious adverse event.

Notes: Percentages were based on the number of subjects in each group in the Safety Population.

AEs were considered to be related to procedure/device, unless the relationship was “not related.” AEs with missing relationship were considered to be related.

All device-related AEs per investigator assessment (i.e., ADEs) are summarized by SOC and PT in Table 12. Overall, 5 (9.4%) subjects experienced at least 1 device-related AE per investigator assessment (5 events). The percentage of subjects with device-related AEs per investigator assessment was 4.0% in the ETHIZIA treatment group (1 event in 1 subject) and 14.3% in the SURGICEL Original treatment group (4 events in 4 subjects). All device-related AEs per investigator assessment were from the PT of application site haemorrhage. All device-related AEs per investigator assessment were considered AESIs.

Table 12. Device-related Adverse Events Per Investigator Assessment by System Organ Class and Preferred Term (Safety Population)

System Organ Class Preferred Term	ETHIZIA (N = 25) n (%) e	SURGICEL Original (N = 28) n (%) e	Overall (N = 53) n (%) e
At least 1 device-related AE per investigator assessment	**1 (4.0) 1**	**4 (14.3) 4**	**5 (9.4) 5**
General disorders and administration site conditions	**1 (4.0) 1**	**4 (14.3) 4**	**5 (9.4) 5**
Application site haemorrhage	1 (4.0) 1	4 (14.3) 4	5 (9.4) 5

Abbreviations: AE, adverse event; e, event count; MedDRA, Medical Dictionary for Regulatory Activities; N, number of subjects in the Safety Population; n, number of subjects with available data in each category.

Notes: Percentages were based on the number of subjects in each group in the Safety Population.

AEs were coded using MedDRA v28.0.

Serious Adverse Events

All Serious Adverse Events (SAEs) are summarized by system organ class (SOC) and PT in Table 13 below.

Overall, 6 (11.3%) subjects experienced at least 1 SAE (10 events). The percentage of subjects with SAEs was 16.0% in the ETHIZIA treatment group (5 events in 4 subjects) and 7.1% in the SURGICEL Original treatment group (5 events in 2 subjects).

The most commonly recorded SAE SOC in the ETHIZIA treatment group was vascular disorders (8.0% of subjects; 2 subjects with 1 event each); all other SAE SOCs occurred in ≤ 1 subject. In the SURGICEL Original treatment group, all SAE SOCs occurred in ≤ 1 subject.

There were no AEs leading to death in either treatment group

Across both treatment groups, all SAE PTs occurred as single events.

Table 13. All Serious Adverse Events by System Organ Class and Preferred Term (Safety Population)			
System Organ Class Preferred Term	**ETHIZIA (N = 25) n (%) e**	**SURGICEL Original (N = 28) n (%) e**	**Overall (N = 53) n (%) e**
At least 1 SAE	**4 (16.0) 5**	**2 (7.1) 5**	**6 (11.3) 10**
Vascular disorders	**2 (8.0) 2**	**1 (3.6) 1**	**3 (5.7) 3**
Hypotension	1 (4.0) 1	1 (3.6) 1	2 (3.8) 2
Deep vein thrombosis	1 (4.0) 1	0	1 (1.9) 1
Gastrointestinal disorders	**1 (4.0) 1**	**1 (3.6) 1**	**2 (3.8) 2**
Vomiting	1 (4.0) 1	1 (3.6) 1	2 (3.8) 2
Respiratory, thoracic and mediastinal disorders	**1 (4.0) 1**	**1 (3.6) 1**	**2 (3.8) 2**
Acute respiratory failure	0	1 (3.6) 1	1 (1.9) 1
Pulmonary embolism	1 (4.0) 1	0	1 (1.9) 1
Blood and lymphatic system disorders	**0**	**1 (3.6) 1**	**1 (1.9) 1**
Blood loss anaemia	0	1 (3.6) 1	1 (1.9) 1
General disorders and administration site conditions	**1 (4.0) 1**	**0**	**1 (1.9) 1**
Non-cardiac chest pain	1 (4.0) 1	0	1 (1.9) 1
Injury, poisoning and procedural complications	**0**	**1 (3.6) 1**	**1 (1.9) 1**
Procedural pain	0	1 (3.6) 1	1 (1.9) 1
Abbreviations: AE, adverse event; e, event count; MedDRA, Medical Dictionary for Regulatory Activities; N, number of subjects in the Safety Population; n, number of subjects with data available in each category; SAE, serious adverse event. Notes: Percentages were based on the number of subjects in each group in the Safety Population. AEs were coded using MedDRA v28.0.			

Adverse Events of Special Interest

The following AESI categories were defined for this trial: bleeding-related events (4 events in ETHIZIA treatment group, 7 in SURGICEL Original treatment group), thromboembolic events (1 event in ETHIZIA treatment group, 0 in SURGICEL Original treatment group), biloma (1 event in ETHIZIA treatment group, 0 in SURGICEL Original), and allergic reaction (0 events).

Of the AESIs, only bleeding-related AESIs were considered to have a (possible) relationship with the device:

- Application site hemorrhage:

Three (12.0%) subjects from the ETHIZIA treatment group experienced a bleeding-related AESI under the PT of application site hemorrhage (3 events). The AESIs of application sites were non-serious. Two of the AESIs were considered not related to the device per investigator assessment and 1 event was considered to be causally related to the investigator assessment.

Four (14.3%) subjects from the SURGICEL Original treatment group experienced a bleeding-related AESI under the PT of application site hemorrhage (4 events). The AESIs of application site hemorrhages were non-serious. The AESIs was considered probably related to the device per investigator assessment (2 events) or causally related per investigator assessment (2 events).

- Abnormal uterine bleeding:

  Not applicable for ETHIZIA.

  One (3.6%) subject from the SURGICEL Original treatment group experienced a bleeding-related AESI under the PT of abnormal uterine bleeding. The AESI of abnormal uterine bleeding was non-serious. Causality to the device was excluded by the investigator (i.e., identified as not related).

- Blood loss anemia:

  Not applicable for ETHIZIA.

  One (3.6%) subject from the SURGICEL Original treatment group experienced a bleeding-related AESI under the PT of blood loss anaemia, which occurred during surgery and was described as acute blood loss anemia from multiple venous branches within the liver parenchyma despite inflow control to the right liver. The AESI of blood loss anaemia was serious. Causality to the device was excluded by the investigator (i.e., identified as not related).

- Incision site discharge:

  Not applicable for ETHIZIA.

  One (3.6%) subject from the SURGICEL Original treatment group experienced a bleeding-related AESI under the PT of incision site discharge. The AESI of incision site discharge was non-serious. Causality to the device was excluded by the investigator (i.e., identified as not related).

- Intra-abdominal hematoma:

  One (4.0%) subject from the ETHIZIA treatment group experienced a bleeding-related AESI under the PT of intra-abdominal haematoma. The AESI of intra-abdominal haematoma was non-serious. Causality to the device was excluded by the investigator (i.e., identified as not related).

  Not applicable for SURGICEL Original.

Exploratory Endpoint results:

No subjects in the ETHIZIA treatment group had a conversion from minimally invasive to open surgery. One (3.6%) subject in the SURGICEL Original treatment group had a conversion from minimally invasive (laparoscopic surgery) to open surgery. The conversion was not due to issues with hemostasis at the target bleeding site or the hemostatic patch.

No subjects in the ETHIZIA treatment group required the addition of a hand port. Two subjects in the SURGICEL Original treatment group required the addition of a hand port. These additions were not due to issues with hemostasis at the target bleeding site or the hemostatic patch.

The mean duration of the procedure was similar across the treatment groups (ETHIZIA treatment group: 164.7 minutes; SURGICEL Original treatment group: 170.9 minutes).

Most subjects were not treated with a hepatic blood inflow reduction method (ETHIZIA treatment group: 72.0%; SURGICEL Original treatment group: 75.0%); for the remainder, the Pringle maneuver was the hepatic blood inflow reduction method used (ETHIZIA treatment group: 28.0%; SURGICEL Original treatment group: 25.0%), with a mean duration of which was shorter in the SURGICEL Original treatment group (ETHIZIA treatment group: 38.1 minutes; SURGICEL Original treatment group: 27.9 minutes).

The mean estimated total blood loss during surgery was similar across the treatment groups (ETHIZIA treatment group: 270.8 mL; SURGICEL Original treatment group: 226.4 mL). The means in both treatment groups were impacted by 2 subjects (1 in each treatment group) with high total intraoperative blood losses (≥ 2000 mL), unrelated to the randomized treatment.

There were 3 subjects that required transfusions during hospitalization after surgery. In the ETHIZIA treatment group, 2 (8.0%) subjects were administered red blood cell transfusions. In the SURGICEL Original treatment group, 1 (3.6%) subject was administered red blood cell and plasma transfusions.

In the ETHIZIA treatment group, no (0%) subjects were admitted to the ICU following surgery, compared to 2 (7.1%) subjects in the SURGICEL Original treatment group, with the admitted subjects staying between 1 to 4 days in the ICU.

The number of subjects requiring hospitalization following surgery was similar across the treatment groups (21 [84.0%] subjects in the ETHIZIA treatment group and 24 [85.7%] subjects in the SURGICEL Original treatment group). For subjects hospitalized following surgery, the total median hospitalization time was the same for subjects in the ETHIZIA treatment group (3.8 days) and the SURGICEL Original treatment group (3.9 days).

A lower proportion of subjects in the ETHIZIA treatment group (36.0%) required a drain to be placed during surgery compared to the SURGICEL Original treatment group (46.4%). The median (minimum, maximum) postoperative drainage duration was similar for the ETHIZIA treatment group (43.5 [4, 172] hours) and the

SURGICEL Original treatment group (48.0 [1, 240] hours). The median (minimum, maximum) volume of drainage was higher for the ETHIZIA treatment group (226.0 [99, 780] mL), compared to the SURGICEL Original treatment group (160.0 [10, 669] mL). Characteristics of postoperative drained fluid were similar for both treatment groups, with serosanguinous being the most common characteristic across both treatment groups. The median (minimum, maximum) bilirubin measured in drainage fluid was similar for the ETHIZIA treatment group (0.90 [0.4, 1.0] mg/dL), compared to the SURGICEL Original treatment group (0.90 [0.50, 1.6] mg/dL).

No subjects underwent reoperation as a result of an SAE.

At Week 6 imaging, there were no instances of device encapsulation, devices rolling up, or formations of pseudoaneurysms on the resection surface in either treatment group. Perihepatic fluid collections were observed in 33.3% of subjects in the ETHIZIA treatment group and 23.1% of subjects in the SURGICEL Original treatment group, with the median (minimum, maximum) size of the perihepatic fluid collections being larger in the ETHIZIA treatment group (ETHIZIA: 50.0 [4.00, 208.98] mL; SURGICEL Original: 25.0 [5.00, 25.00] mL). The most frequent perihepatic fluid collection impression was ‘nonspecific’ (5 [23.8%] subjects in the ETHIZIA treatment group; 5 [19.2%] subjects in the SURGICEL Original treatment group). None of the perihepatic fluid collections were considered to be clinically relevant.

The amount of hemostatic material needed per subject (i.e., the total number of number of hemostatic patches introduced through the trocar per subject across all target bleeding sites) was similar across the treatment groups; the median (minimum, maximum) number of hemostatic patches needed was 0.63 (0.33, 2.33) in the ETHIZIA treatment group and 1.0 (0.25, 2.00) in the SURGICEL Original treatment group.

For the ETHIZIA usability scale, surgeons agreed that they would use the ETHIZIA frequently (96.0%), that it was easy to use (92.0%), that the various functions in the ETHIZIA were well integrated (84.0%), and that most other surgeons would learn to use it very quickly (88.0%). According to most questionnaires, surgeons disagreed that it was unnecessarily complex (92.0%), that they would need technical support to be able to use it (92.0%), that the product was inconsistent (92.0%), or that it was cumbersome (96.0%).

For the user satisfaction per the medical device-specific questions, in most questionnaires, users either agreed or strongly agreed with the medical device-specific questions. The lowest score obtained was for Question 12 (“A dry ETHIZIA does not stick to dry gloves and instruments”), where agreed or strongly agreed was the response in 88.0% of the answers, with all other questions being answered with agreed or strongly agreed in ≥ 92.0%.

2. Effectiveness Results

Primary effectiveness endpoint:

The analysis of effectiveness was based on the 53 evaluable patients at the 12-week time point. Key effectiveness outcomes are presented in Tables 14 to 17.

The primary endpoint was defined as the delivery and adherence of the agent to the first target bleeding site and achievement of hemostasis within 7 minutes from introduction of the first (piece of) patch through the trocar, without rebleeding at the 10-minute assessment from initiating pressure on the hemostatic agent, and without the need to convert the surgical approach or use a handport due to issues with hemostasis at the target bleeding site or device use.

In the mITT population, among first target bleeding sites for each subject, the subject-level responder rate for the ETHIZIA group was 25/25 (100%) compared to the subject-level responder rate for the SURGICEL Original group 23/28 (82%). One ETHIZIA responder subject received rescue therapy (15 minutes after introducing the first (piece of) hemostatic agent through the trocar but prior to closure) on their first target bleeding site after primary endpoint evaluation.

As a supportive analysis, the results of the primary efficacy endpoint of the achievement of hemostasis for the first target bleeding site were also summarized for the PP Population. Table 14 provides the data for the primary endpoint for both mITT and PP populations.

Table 14. Primary Efficacy Endpoints		
First Target Bleeding Site		
Achievement of Hemostasis Primary Efficacy Analysis Target Bleeding Site	**ETHIZIA n (%)**	**SURGICEL Original n (%)**
Primary Endpoint Success (Achieving hemostasis at 7 min from introduction of the first (piece of) patch through the trocar without rebleeding at the 10-minutes timepoint from initiating pressure on the entire surface of the hemostatic agent and without the use of a hand port or need to convert the surgical approach to open surgery, first bleeding site) **(mITT Population)**	**N=25** 25 (100)	**N=28** 23 (82)[a]
Primary Endpoint Success (Achieving hemostasis at 7 min from introduction of the first (piece of) patch through the trocar without rebleeding at the 10-minutes timepoint from initiating pressure on the entire surface of the hemostatic agent and without the use of a hand port or need to convert the surgical approach to open surgery, first bleeding site) **(PP Population)**	**N=24** 24 (100)	**N=27** 23 (85)

Table 14. Primary Efficacy Endpoints		
First Target Bleeding Site		
Achievement of Hemostasis Primary Efficacy Analysis Target Bleeding Site	**ETHIZIA n (%)**	**SURGICEL Original n (%)**
Abbreviations: mITT, modified intent-to-treat; N, number of subjects in the ITT Population; n, number of subjects used for the analysis; PP, per-protocol. a. Site 999 only randomized 1 subject (SURGICEL Original treatment group) for whom no primary efficacy endpoint data were collected; thus, it was not possible to determine a primary efficacy endpoint success for this subject, and the subject was considered missing for outcome (success/failure) but included in the denominator for the analysis according to the mITT framework. This subject is removed from the PP analysis.		

Key secondary effectiveness endpoint

The key secondary effectiveness endpoint was the median time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis (seconds).

In the mITT population for first target bleeding sites, the median time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis was 100 seconds (range 40-343 seconds) in the ETHIZIA treatment group compared to 88 seconds (range 37-1217 seconds) in the SURGICEL Original treatment group, see Table 15.

For analyses conducted on both the first target bleeding site and all target bleeding sites, the results of the supportive analyses conducted on the PP Population and the main analyses conducted on the mITT Population showed the same direction of treatment effect in both populations, supporting the consistency of the observed outcomes.

Table 15. Key Secondary Endpoint (mITT Population)			
First Target Bleeding Site			
	Statistic	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**
Number of First Target Bleeding Sites	**n**	**25**	**28**
Time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis (seconds)	n	25	27[a]
	Mean (SD)	126 (82)	187 (268)
	Median	100	88
	Min, Max	40, 343	37, 1217
Censored[a,b,c,d]	n (%)	0	5 (17.9)
Uncensored	n (%)	25 (100)	23 (82.1)

Table 15. Key Secondary Endpoint (mITT Population)			
First Target Bleeding Site			
	Statistic	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**

Abbreviations: mITT, modified intent-to-treat; Max, maximum; Min, minimum; N, number of subjects in the mITT Population; n, number of subjects in the category; SD, standard deviation.

a. One subject in the SURGICEL Original treatment group, did not have hemostasis data and hence, this subject was censored at Time=0.
b. Time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis was censored at 15 minutes, in subjects who did not achieve hemostasis after 10 minutes from initiating pressure.
c. For subjects who achieved hemostasis with additional patch and time to hemostasis was after 10 minutes from initiating pressure, then the time was censored at 15 minutes.
d. For subjects who received rescue therapy, time to hemostasis ≤ 15 minutes from introducing through the trocar was censored at 15 minutes and time to hemostasis after 10 minutes from initiating pressure was also censored at 15 minutes
e. The Kaplan Meier method was used to derive the percentiles and its CIs

Other Secondary Endpoints

The median time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the hemostatic agent at the first target bleeding site, was 57 seconds (range 10-295 seconds) for the ETHIZIA treatment group compared to 29 seconds (range 7-95 seconds) for the SURGICEL Original treatment, as presented in Table 16. Results for the time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the hemostatic agent for all target bleeding sites were similar to the results for the first target bleeding site (see Table 18 Summary of Effectiveness for All Treated Target Bleeding Sites).

The median time to hemostasis from initiating pressure on the entire surface of the hemostatic agent at the first target bleeding site, was similar across the ETHIZIA treatment group (30 seconds) and the SURGICEL Original treatment group (30 seconds). However, the mean (SD), as well as the minimum and maximum values, indicated that ETHIZIA was faster in achieving hemostasis once positioned and pressure initiated for the first target bleeding site. Results for time to hemostasis from initiating pressure on the entire surface of the hemostatic agent for all target bleeding sites were similar to the results for the first target bleeding site (See Table 18 Summary of Effectiveness for All Treated Target Bleeding Sites).

Treatment failure for the first target bleeding site is summarized descriptively in Table 16 for the mITT Population. The percentage of subjects with treatment failure at 10 minutes for the first target bleeding site was 0% in the ETHIZIA treatment group and 14.3% in the SURGICEL Original treatment group (n=4/28 subjects). The

number of subjects requiring rescue treatment for the first target bleeding site within 10 minutes of initiating pressure on the first (piece of) hemostatic agent was correspondingly low: no (0%) subjects in the ETHIZIA treatment group and 4 (14.3%) subjects in the SURGICEL Original treatment group; the majority of subjects in the SURGICEL Original treatment group who needed additional surgical techniques or hemostatic agents for the first target bleeding site within 10 minutes of initiating pressure on the first (piece of) hemostatic agent received electrocautery (75%; n=3/4 subjects).

In the SURGICEL Original treatment group, none of the target bleeding sites had rebleeding after the 10-minute timepoint from initiating pressure on the entire surface of the hemostatic agent but before subject wound closure. In the ETHIZIA treatment group, 1 of the target bleeding sites had rebleeding after the 10-minute time point; this rebleeding occurred in a subject at their first target bleeding site (see Table 16 Other Secondary Endpoints). Neither surgeon nor sponsor determined the rebleeding to occur due to the patch or application of the patch.

Six (24.0%) subjects in the ETHIZIA treatment group and two (7.1%) subjects in the SURGICEL Original treatment group received an additional piece of hemostatic agent to attempt achieving hemostasis at the first target bleeding site; all these subjects received 1 additional piece of hemostatic agent (see Table 16 Other Secondary Endpoints).

Table 16. Other Secondary Endpoints (mITT)

First Target Bleeding Site

Secondary efficacy endpoints	**Statistic**	**ETHIZIA (N=25)**	**SURGICEL Original (N=28)**
Time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the agent (seconds)	N Mean (SD) Median Min, Max Censored [n (%)] Uncensored [n (%)]	25 74 (59) 57 10, 295 0 25 (100)	27[a] 40 (27) 29 7, 95 4 (14.2) 24 (85.7)
Time to hemostasis from initiating pressure on the entire surface of the agent (seconds)	N Mean (SD) Median Min, Max Censored [n (%)] Uncensored [n (%)]	25 52 (64) 30 30, 300 0 25 (100)	27[a] 147 (261) 30 30, 1122 5 (17.9) 23 (82.1)
Treatment failure, defined as no hemostasis with the agent at 10 minutes from initiating pressure on the entire surface of the agent;	N Treatment failure – N (%) Rescue therapy – N (%) Electrocautery – N (%) Surgiflo – N (%)	25 0 0 0 0	28 4 (14.3) 4 (14.3) 3 (75.0) 1 (25.0)

Table 16. Other Secondary Endpoints (mITT)			
First Target Bleeding Site			
Secondary efficacy endpoints	**Statistic**	**ETHIZIA (N=25)**	**SURGICEL Original (N=28)**
Rebleeding after the 10-minute time point from initiating pressure on the entire surface of the agent but before subject wound closure;	N Rebleeding after 10 min – N (%)	25 1 (4)	28 0
Number of times an additional (piece of) hemostatic agent needs to be used to achieve hemostasis.	1 2 ≥ 3	19 (76.0) 6 (24.0) 0	26 (92.9) 2 (7.1) 0
Abbreviations: CI, confidence interval; mITT, modified intent-to-treat; Max, maximum; Min, minimum; N, number of subjects in the mITT Population; n, number of subjects in the category; SD, standard deviation. [a.] Subject 999-002, from the SURGICEL Original treatment group, did not have hemostasis data and hence, this subject was censored at Time=0.			

A Kaplan Meier plot of time to hemostasis from initiating pressure on the entire surface of the hemostatic agent at the first target bleeding site is shown in Figure 2 for the mITT population.

Hemostasis following initiation of pressure on the agent at the first target bleeding site was achieved for all 25/25 (100%) subjects in the ETHIZIA treatment group at 300 seconds and 23/28 (82.1%) in SURGICEL Original subjects. In the SURGICEL Original treatment group, 1 subject did not have hemostasis data and was censored at Time 0. Four subjects were censored at 600 seconds (i.e., did not achieve hemostasis by 10 minutes or rescue therapy was used).

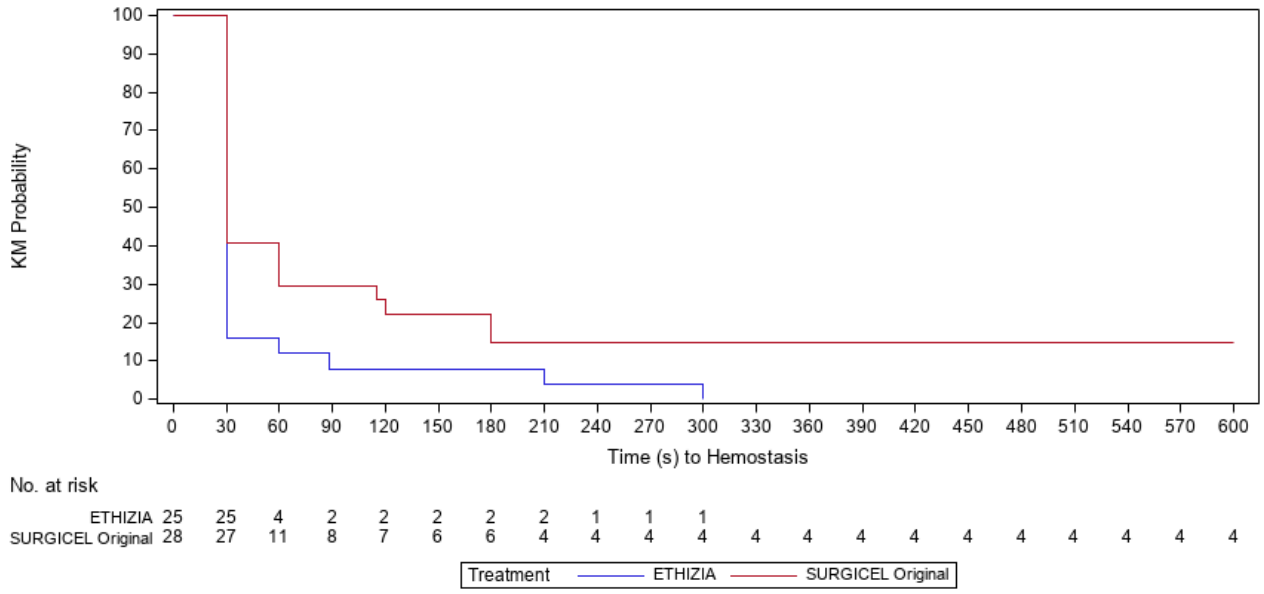


Figure 2: Kaplan-Meier estimated distribution of time to hemostasis from initiating pressure on the entire surface of the agent – First Target Bleeding site

The percentage of subjects with hemostasis from initiating pressure on the entire surface of the hemostatic agent at 30, 60, 120, 180, 240, 300, 360, 420, 480, 540, and 600 seconds at the first target bleeding site, and maintaining hemostasis up to 10 minutes, is summarized descriptively in Table 17 for the mITT Population.

In the ETHIZIA treatment group, hemostasis after initiating pressure on the agent at the first target bleeding site was achieved in 84.0% (21/25) of subjects at 30 seconds, 88.0% (22/25) of subjects at 60 seconds, and 100% (25/25) of subjects at 300 seconds compared to 57.1% (16/28) of subjects at 30 seconds, 67.9% (19/28) of subjects at 60 seconds, and 82.1% (23/28) of subjects at 300 seconds in the SURGICEL Original treatment group. After reaching the maximum attained hemostasis of 82.1% of subjects at 180 seconds, no additional hemostasis was achieved by subjects in the SURGICEL Original treatment group up to 600 seconds. Results for the percentage of all target bleeding sites achieving hemostasis at each time point were similar to the results based on the first target bleeding site (see Table 18 for all Treated Target Bleeding Sites).

Table 17. Percentage Subjects with Hemostasis From Initiating Pressure on the Entire Surface of the Hemostatic Agent at 30, 60, 120, 180, 240, 300, 360, 420, 480, 540, and 600 Seconds (mITT Population)

First Target Bleeding Site	Statistic	ETHIZIA (N = 25)	SURGICEL Original (N = 28)
Number of subjects who achieved hemostasis from initiating pressure on the entire surface of the hemostatic agent to 10 minutes	n	25	23
Subjects who achieved hemostasis at:			
30 seconds	n (%)	21 (84.0)	16 (57.1)
60 seconds	n (%)	22 (88.0)	19 (67.9)
120 seconds	n (%)	23 (92.0)	21 (75.0)
180 seconds	n (%)	24 (96.0)	23 (82.1)
240 seconds	n (%)	24 (96.0)	23 (82.1)
300 seconds	n (%)	25 (100)	23 (82.1)
360 seconds	n (%)	25 (100)	23 (82.1)
420 seconds	n (%)	25 (100)	23 (82.1)
480 seconds	n (%)	25 (100)	23 (82.1)
540 seconds	n (%)	25 (100)	23 (82.1)
600 seconds	n (%)	25 (100)	23 (82.1)

Abbreviations: mITT, modified intent-to-treat; N, number of subjects in the ITT Population; n, number of subjects with available data in each category; PP, per-protocol.

Notes: Subjects who received rescue therapy before 10-min post-initiating pressure on the entire surface of the agent were considered as treatment failure and thus were not counted as achieving hemostasis in this analysis, but they were still included in the denominator according to the mITT framework. Additionally, for one subject in the SURGICEL Original treatment group, hemostasis and bleeding site information was not collected and, therefore, considered missing for outcome (success/failure) but the subject was included in the denominator for the analysis according to the mITT framework.

A supportive analysis of the primary endpoint was conducted on the level of all target bleeding sites in the mITT population. The target bleeding site-level responder rate for the ETHIZIA treatment group was 33/35 (94%) compared to the target bleeding site-level responder rate for the SURGICEL Original treatment group 24/29 (83%). The same supportive analysis was conducted on the PP Population. Results for hemostasis across all treated target bleeding sites are summarized in Table 18.

In the mITT population for all target bleeding sites, the median time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis was 100 seconds in the ETHIZIA group and 87 seconds in the SURGICEL Original group (Table 18).

Table 18: Summary of Effectiveness Results for All Treated Target Bleeding Sites

Primary Efficacy Endpoint - All Treated Target Bleeding Sites	ETHIZIA n (%)	SURGICEL Original n (%)
Primary Endpoint Success (Achieving hemostasis at 7 min from introduction of the first (piece of) patch through the trocar without rebleeding at the 10-minutes timepoint from initiating pressure on the entire surface of the hemostatic agent and without the use of a hand port or need to convert the surgical approach to open surgery, first bleeding site) **(mITT Population)**	**N=35**[a] 33 (94)[b]	**N=29**[a] 24 (83)[b]
Primary Endpoint Success (Achieving hemostasis at 7 min from introduction of the first (piece of) patch through the trocar without rebleeding at the 10-minutes timepoint from initiating pressure on the entire surface of the hemostatic agent and without the use of a hand port or need to convert the surgical approach to open surgery, first bleeding site) **(PP Population)**	**N=34**[a] 32 (94)[b]	**N=28**[a] 24 (86)[b]

a. Number of bleeding sites across all subjects in the treatment group.
b. Number and percentage (%) of bleeding sites with hemostasis achieved within 7 minutes without rebleeding at 10 minutes and without converting approach or using hand port across all subjects in the treatment group.

Key Secondary Endpoint – All Treated Target Bleeding Sites (mITT Population)	Statistic	ETHIZIA (N = 25)	SURGICEL Original (N = 28)
Number of All Treated Target Bleeding Sites	**n**[a]	**35**	**29**
Time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis (seconds)	n[b]	34[c]	28[d]
	Mean (SD)	149 (200)	182 (264)
	Median	100	87
	Min, Max	40, 1200	37, 1217
Censored[c,d,e,f,g]	n (%)[h]	2 (5.7)	5 (17.2)
Uncensored	n (%)[h]	33 (94.3)	24 (82.8)

a. Number of bleeding sites across all subjects in the treatment group.
b. Number bleeding sites with hemostasis achieved across all subjects in the treatment group.
c. The second target bleeding site for one subject in the ETHIZIA treatment group, was excluded from this descriptive analysis because the time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis was not recorded. For this bleeding site, both patches were attempted to be applied but neither adhered as they become too soiled with blood and were subsequently removed; the subject subsequently received rescue treatment of electrocautery at this bleeding site.
d. One subject in the SURGICEL Original treatment group, did not have hemostasis data for their first target bleeding site.

Table 18: Summary of Effectiveness Results for All Treated Target Bleeding Sites

e. Time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis was censored at 15 minutes for bleeding sites which did not achieve hemostasis after 10 minutes from initiating pressure.
f. For bleeding sites which achieved hemostasis with additional patch and the time to hemostasis was after 10 minutes from initiating pressure, then the time was censored at 15 minutes.
g. For bleeding sites which required rescue therapy, time to hemostasis ≤ 15 minutes from introducing through the trocar was censored at 15 minutes and time to hemostasis after 10 minutes from initiating pressure was also censored at 15 minutes.
h. Percentages were based on the number of all target bleeding sites in each group.

Other Secondary Endpoints – All Treated Target Bleeding Sites (mITT Population)	**Statistic**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**
Number of All Target Bleeding Sites	**n[a]**	**35**	**29**
Time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the hemostatic agent (seconds)	n[b]	34[c]	28[d]
	Mean (SD)	67 (54)	39 (27)
	Median	51	29
	Min, Max	10, 295	7, 95
Censored[c,d,e]	n (%)	2 (5.7)	4 (13.8)
Uncensored	n (%)	33 (94.3)	25 (86.2)

a. Number of all target bleeding sites across all subjects in the treatment group.
b. Number of bleeding sites with available data across all subjects in the treatment group.
c. One subject in the ETHIZIA treatment group had a second bleeding site that did not have the time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the hemostatic agent recorded, and, thus, was not included in the descriptive analysis. However, hemostasis achieved status (yes/no) was recorded, and it was also recorded that the subject received rescue treatment at this bleeding site.
d. One subject in the SURGICEL Original treatment group, did not have hemostasis data for their first target bleeding site.
e. Time from introducing the first (piece of) hemostatic agent through the trocar to initiating pressure on the entire surface of the hemostatic agent (seconds) was censored for bleeding sites where the patch could not be successfully positioned.

Other Secondary Endpoints – All Treated Target Bleeding Sites (mITT Population)	**Statistic**	**ETHIZIA (N = 25)**	**SURGICEL Original (N = 28)**
Number of All Target Bleeding Sites	**N[a]**	**35**	**29**
Time to hemostasis from initiating pressure on the entire surface of the hemostatic agent (seconds)	N[b]	33[c]	28[d]
	Mean (SD)	48 (56)	143 (257)
	Median	30	30
	Min, Max	30, 300	30, 1122

Table 18: Summary of Effectiveness Results for All Treated Target Bleeding Sites			
Censored[c,d,e,f,g]	n (%)	2 (5.7)	5 (17.2)
Uncensored	n (%)	33 (94.3)	24 (82.8)

Abbreviations: mITT, modified intent-to-treat; Max, maximum; Min, minimum; n, number of subjects in the category; SD, Standard Deviation.

a. Number of all target bleeding sites across all subjects in the treatment group.
b. Number of bleeding sites with available data across all subjects in the treatment group.
c. For 2 subjects in the ETHIZIA treatment group, both had a second bleeding site that did not have the time to hemostasis from initiating pressure on the entire surface of the hemostatic agent recorded and, thus, were not included in the descriptive analysis. However, hemostasis achieved status (yes/no) was recorded and it was also recorded that both subjects received rescue treatment at these bleeding sites; therefore, data for these subjects' second target bleeding were censored.
d. One subject in the SURGICEL Original treatment group, did not have hemostasis data for their first target bleeding site.
e. Time to hemostasis from initiating pressure on the entire surface of the hemostatic agent was censored at 10 minutes for bleeding sites which did not achieve hemostasis by 10 minutes.
f. For bleeding sites which achieved hemostasis with additional patch and time to hemostasis was after 10 minutes, then the time was censored at 10 minutes.
g. For bleeding sites which required rescue therapy, time to hemostasis ≤ 10 minutes from initiating pressure was censored at 10 minutes and time to hemostasis after 10 minutes from initiating pressure was also censored at 10 minutes.

In the ETHIZIA treatment group, hemostasis after initiating pressure on the agent at all target bleeding site was achieved in 77.1% (27/35) of bleeding sites at 30 seconds, 85.7% (30/35) of bleeding sites at 60 seconds, and 91/4% (32/35) of bleeding sites at 180 seconds compared to 58.6% (17/29) of bleeding sites at 30 seconds, 69.0% (20/29) of bleeding sites at 60 seconds, and 82.8% (24/29) of bleeding sites at 180 seconds in the SURGICEL Original treatment group (Table 19).

Table 19. Percentage Subjects with Hemostasis From Initiating Pressure on the Entire Surface of the Hemostatic Agent at 30, 60, 120, 180, 240, 300, 360, 420, 480, 540, and 600 Seconds (mITT Population)

All Treated Target Bleeding Sites	Statistic	ETHIZIA (N=25)	SURGICEL Original (N=28)
Number of All Target Bleeding Sites	**n[a]**	**35**	**29**
Number of all target bleeding sites which achieved hemostasis from initiating pressure on the entire surface of the hemostatic agent to 10 minutes	n[b]	33	24
All target bleeding sites which achieved hemostasis at:			
30 seconds	n[b] (%)	27 (77.1)	17 (58.6)
60 seconds	n[b] (%)	30 (85.7)	20 (69.0)
120 seconds	n[b] (%)	31 (88.6)	22 (75.9)
180 seconds	n[b] (%)	32 (91.4)	24 (82.8)
240 seconds	n[b] (%)	32 (91.4)	24 (82.8)
300 seconds	n[b] (%)	33 (94.3)	24 (82.8)
360 seconds	n[b] (%)	33 (94.3)	24 (82.8)
420 seconds	n[b] (%)	33 (94.3)	24 (82.8)
480 seconds	n[b] (%)	33 (94.3)	24 (82.8)
540 seconds	n[b] (%)	33 (94.3)	24 (82.8)
600 seconds	n[b] (%)	33 (94.3)	24 (82.8)

Abbreviations: mITT, modified intent-to-treat; N, number of subjects in the mITT Population.

[a] Number of all target bleeding sites across all subjects in the treatment group.

[b] Number of bleeding sites with hemostasis achieved all subjects in the treatment group.

Notes: All treated bleeding sites requiring rescue therapy were considered as treatment failures and thus were not counted as achieving hemostasis in this analysis, but they were still included in the denominator according to the mITT framework. Additionally, for one subject, hemostasis and bleeding site information was not collected and, therefore, considered missing for outcome (success/failure) but the subject's bleeding site was included in the denominator for the analysis according to the mITT framework.

Percentages were based on number of all target bleeding sites in each group.

Subgroup analysis

The following baseline characteristics were evaluated for potential association with the safety and effectiveness outcomes: sites, type of MIS, surgeon experience. Subgroup analyses were investigated for the primary effectiveness endpoint of the achievement of hemostasis at the first target bleeding site per the subgroups. The achievement of hemostasis at the first target bleeding site is summarized descriptively in Table 20 by type of MIS, by surgeon experience level, and by trial site for the mITT Population. Although there was some variation seen in specific subgroups, subject numbers tended to be relatively small and thereby analyses were inconclusive, rendering the treatment effect consistent across subgroups.

Table 20. Subgroup Analyses – Primary Efficacy Endpoint (Achievement of Hemostasis) for the First Target Bleeding Site (mITT Population)

Subgroup	ETHIZIA n/N (%) Response Rate	SURGICEL Original n/N (%) Response Rate
Trial site		
994	3/3 (100)	3/4 (75)
995	4/4 (100)	3/5 (60)
996	7/7 (100)	6/7 (86)
997	4/4 (100)	4/4 (100)
998	7/7 (100)	7/7 (100)
999	0/0 NE	0/1[a] NE)
Type of MIS		
Laparoscopic	8/8 (100)	7/8 (88)
Robotic	17/17 (100)	16/20[b] (80)
Surgeon Experience Level[b]		
1 to 20 years	12/12 (100)	10/14 (71)
21 to 44 years	13/13 (100)	13/14[b] (93)

Abbreviations: CI, confidence interval; mITT, modified intent-to-treat; MIS, minimally invasive surgery; N, total number of subjects in the treatment group within the subgroup; n, number of subjects with hemostasis achieved within 7

Table 20. Subgroup Analyses – Primary Efficacy Endpoint (Achievement of Hemostasis) for the First Target Bleeding Site (mITT Population)		
Subgroup	**ETHIZIA n/N (%) Response Rate**	**SURGICEL Original n/N (%) Response Rate**
minutes without rebleeding at 10 minutes and without converting approach or using hand port. [a.] Site 999 only randomized 1 subject (from the SURGICEL Original treatment group) for whom no primary efficacy endpoint data were collected; thus, it was not possible to determine a primary efficacy endpoint success rate or difference for Site 999. [b.] Site 999 only randomized 1 subject (from the SURGICEL Original treatment group) for whom no primary efficacy endpoint data were collected; thus, it was not possible to determine a primary efficacy endpoint success for this subject, and the subject was considered missing for outcome (success/failure) but included in the denominator for the analysis according to the ITT framework. Notes: Response Rate = (Number of subjects with hemostasis achieved within 7 minutes without rebleeding at 10 minutes and without converting approach or using hand port)/(Total number of subjects in that treatment group). To calculate the response rate and the corresponding 95% CI, the exact (Clopper-Pearson) method was used. For the calculation of difference of response rate between treatment group and the corresponding 95% CI, Newcombe method was used.		

3. Pediatric Extrapolation

   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included six (6) investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Devices Panel, an FDA advisory committee, for review and recommendation

because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness results of ETHIZIA demonstrate that the device is effective for minimally invasive surgical procedures on the liver. The MIS study (G230105) was descriptive, but ETHIZIA has met all pre-specified primary and secondary effectiveness endpoints.

The primary endpoint of delivery and adherence of the agent to the target bleeding site and achievement of hemostasis within 7 minutes from introduction of the first patch through the trocar without rebleeding at the 10-minute timepoint was 100.0% (25/25) for ETHIZIA and 82.0% (23/28) for SURGICEL Original. Among the 25 ETHIZIA patients, there were 35 target bleeding sites treated, and hemostasis was achieved in 30 seconds from initiating pressure in 77.1% (27/35), in 60 seconds in 85.7% (30/35), and in 3 minutes in 91.4% of bleeding sites. The median time to hemostasis from initiating pressure was 30 seconds for both ETHIZIA and SURGICEL Original.

For the key secondary endpoint, the median time from introducing the first (piece of) hemostatic agent through the trocar and achieving hemostasis was 100 seconds in the ETHIZIA treatment group compared to 88 seconds in the SURGICEL Original treatment group, among all first target bleeding sites.

B. Safety Conclusions

The risks of the device are based on nonclinical animal studies as well as data collected in the MIS clinical study conducted to support PMA approval as described above. Within the MIS pivotal IDE, there were 73 total adverse events in 30 of the 53 (56.6%) patients. Overall, SAEs occurred most frequently in the vascular disorder system class (N=3/53; 5.7%), gastrointestinal disorders (N=2/53; 3.8%) and respiratory, thoracic and mediastinal disorders (N=2/53; 3.8%).

The rate of AEs and SAEs was comparable between the ETHIZIA and SURGICEL Original treatment groups, with fewer subjects in the ETHIZIA treatment group experiencing device-related AEs. All SAEs in both groups were single occurrences. Of the 73 total adverse events, 1/25 (4.0%) patients experienced an event related to ETHIZIA (application site hemorrhage; 1/25; 4.0%), and 4/28 (14.3%) patients in the SURGICEL Original group (application site hemorrhage; 4/28; 14.3%).

The majority of device-related AEs were related to application site hemorrhage. In the ETHIZIA treatment group, the event of application site hemorrhage was considered causally related to ETHIZIA. In the SURGICEL Original treatment group, 2 of the application site hemorrhage events were considered probably related and 2 considered causally related to SURGICEL Original.

Importantly, the rate of bile leakage was low with only a single reported non-serious AE of biloma. There were no deaths, and no subjects required reoperation.

In conclusion, the safety profile of the ETHIZIA Hemostatic Patch was found to be acceptable compared to standard of care regarding the rate and types of device-related adverse events.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in the MIS clinical study conducted to support PMA approval as described above.

The effectiveness endpoint results of the MIS study on subjects undergoing minimally invasive liver resection surgery, showed that 25/25 (100%) of subjects treated with ETHIZIA had met the primary endpoint of delivery and adherence of the agent to the target bleeding site and achievement of hemostasis within 7 minutes from introduction of the first patch through the trocar without rebleeding at the 10-minute timepoint, versus 23/28 (82%) for subjects treated with SURGICEL Original. .

The probable risks of the device are also based on data collected in the MIS clinical study conducted to support PMA approval as described above. Based on the MIS study, the types of adverse events and serious adverse events occurring with ETHIZIA treated patients compared to control groups revealed no increased risk of complications directly attributable to ETHIZIA.

No new or unanticipated adverse effects or patient risks were identified in the MIS study.

Patient Perspective

This submission either did not include specific information on patient perspectives, or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the use of ETHIZIA in minimally invasive surgical procedures as an adjunct to hemostasis when control of minimal, mild, or moderate bleeding by conventional procedures is ineffective or impractical, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of ETHIZIA when used in accordance with the indications for use.

The hemostatic performance of ETHIZIA within the clinical studies demonstrates the benefits of fast and sustained hemostasis resulting in less clinical risk of bleeding related complications. The safety assessments demonstrated no increased risk of complications directly attributable to the device when compared to standard of care.

The data in this application supports the reasonable assurance of ETHIZIA when used in accordance with the indications for use.

XIV. CDRH DECISION

CDRH issued an approval order on June 25, 2026. There are no clinical conditions of approval for the current Panel-Track Supplement. Several clinical conditions of approval have been included in the SSED of the original PMA available on the CDRH website.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XV. APPROVAL SPECIFICATIONS

Directions for use: see the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, warnings, Precautions, and Adverse Reactions in the labeling.

Post-approval Requirements and Restrictions: See Approval Order.