Statistical Analysis Plan

A Prospective, Multicenter, Randomized Controlled Study to Evaluate the Effect of Absorbable Adhesion Barrier in Preventing the Abdominal Incision Site Adhesions

Sponsor	Johnson & Johnson Medical (Shanghai) Ltd.
CRO:	ClinChoice Medical (TIANJIN) Co., Ltd.
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Abbreviations

Abbreviations	Full Name
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
CDC	Centers for Disease Control and Prevention
Clopper-Pearson	A method for estimating the confidence interval for a proportion with small samples based on binomial distribution
CP	Conditional power
DMC	Data Monitoring Committee
INTERCEED	Absorbable adhesion barrier
ITT	Intention-to-treat
MedDRA	Medical Dictionary for Regulatory Activities
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Events
PP	per-protocol
PT	Preferred Term
SAP	Statistical analysis plan
SOC	System Organ Class
SSI	Incidence of surgical site infections
WHODRUG	World Health Organization Drug Dictionary

1 Introduction

This study is a prospective randomized controlled study of Johnson & Johnson Medical (Shanghai) Ltd., the primary objective is to evaluate the efficacy and safety of INTERCEED™ in reducing the incidence of adhesions at the target incision site in patients undergoing laparoscopic colorectal surgery. This Statistical Analysis Plan provides the statistical analysis methods and data processing principles with regard to effectiveness and safety.

This Statistical Analysis Plan is based on the protocol: A Prospective, Multicenter, Randomized Controlled Study to Evaluate the Effect of Absorbable Adhesion Barrier in Preventing the Abdominal Incision Site Adhesions, Version No.: 5.0 (Version Date: April 27, 2020).

1.1 Study Objectives

The primary objective of this study is to evaluate the efficacy and safety of INTERCEED™ in reducing the incidence of adhesions at the target incision site in patients undergoing laparoscopic colorectal surgery.

1.2 Study Endpoints

1.2.1 Primary Efficacy Endpoint

The proportion of subjects free of adhesions at the target incision site in each study group based on evaluation through laparoscopy at ileostomy reversal (phase 2 operation).

1.2.2 Secondary Efficacy Endpoints

a. Extent and severity of adhesions at the target incision site and four abdominal quadrants (see Attachment 7.1)

b. Incidence of mechanical ileus

1.2.3 Safety Endpoints

a. Incidence of surgical site infection (SSI) at the target incision after the phase 1 operation (SSI);

b. Incidence of all layer wound dehiscence of the target incision after Phase 1 operation;

c. Incidence of delayed wound healing of the target incision after Phase 1 operation;

d. Adverse events

1.2.4 Other Endpoints

Product defects of the study product

1.3 Study Design

1.3.1 Overall Design

This is a prospective randomized controlled study. The study will include 220 patients who are scheduled to undergo laparoscopic radical resection of colorectal carcinoma and ileostomy reversal in Phase 2 operation. During the Phase 1 operation, when the definite decision to create

a temporary ostomy was made, patients were randomized in 1:1 ratio to either the treatment arm (INTERCEED™) or the control arm (standard of care: no adhesion barrier, no placebo). In subjects assigned to the treatment arm, INTERCEED™ was applied beneath the target incision site (the midline incision for the removal specimen). The subjects returned 3-9 months after the phase 1 operation (colorectal carcinoma resection with temporary ileostomy) for phase 2 operation (ileostomy reversal) when the incidence, extent and severity of adhesions were evaluated through the laparoscope.. For the study schedule and events table, see Table 1:

Table 1 Study Flow Chart

Item	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7 [h]
Time point	Screening/Baseline: performed whthin 14 days before Phase 1 operation	Randomization :performed during the Phase 1 operation	Phase 1 operation	Post-Op (Phase 1) through Discharge	Phase 2 operation: performed between 3-9 months after Phase 1 operation [a]	3 days after Phase 2 operation or Discharge	6-7months after Phase 1 operation
Informed consent	X						
Demographic information	X						
Randomization		X					
Inclusion/Exclusion Criteria	X	X					
Urine/blood pregnancy test	X						
Medical/Surgical history [b]	X				X		X
Concomitant therapy[c]	X		X	X	X	X	
Physical examination [d]	X			X	X	X	
Concomitant medications[e]	X		X	X	X	X	
Procedural data [f]			X		X		
Mechanical ileus				X	X	X	X
SSI				X	X	X	X
Incision dehiscence				X	X	X	X
Delayed wound healing events				X	X	X	X
Adverse event	X	X	X	X	X	X	X
Defectts of study product			X	X	X	X	X
Study completion [g]						X	X

a. Other information except operative data should be collected from admission to hospital to the day before operation.

b. The surgical history should be collected carefully in the three visits. The medical history at Visit 7 should be included only diagnoses potentially related to abdominal adhesions.

c. The neoadjuvant radiotherapy information should be collected at Screening/Baseline visit, if any. The radiotherapy information includes dose and site.

d. Including height, weight and abdominal sign.

e. Only including the medicine related to adverse events and which is used beyond two weeks. The neoadjuvant/postoperative chemotherapy protocol and period should also be collected.

f. The information about the procedure time, hemorrhage volume, use of sterile gloves, target incision, application of study product in the study group should be collected at the visits of Phase 1 operation; the image data and the treatment for adhesion (if any) should be collected in the Phase 2 operation.

g. If Visit 6 occurs 6-9 months after Phase 1 operation, the study completion would be in Visit 6. If not, the study completion would be in Visit 7.

h. Phone contact. If Visit 6 occurs 3-6 months after Phase 1 operation, the Visit 7 need to be conducted.

1.3.2 Randomization and Blinding

Randomization occurred if the patient met all inclusion criteria and did not meet any exclusion criteria. The stratified randomization method with blocks was adopted, in which neoadjuvant radiotherapy was a stratification factor, and the block size was 4. Each case was randomized to one of two groups in a 1:1 ratio. The only difference between the groups was the use of INTERCEED™ or not.

The Sponsor provided each site with computer-generated randomization envelopes, each bearing the subject randomization number, and containing the treatment allocation. In the event a potential subject failed intra-operative criteria, and was not randomized to the study, the unused randomization envelope was returned to the series, and used for the next subject per its original sequence.

Blinding practices for this study included the following:

Patients: Patients were informed of the 1:1 randomization to determine whether the study product was to be implanted, but remained blinded to study treatment (INTERCEED™ or Control) until they had completed all study follow-up.

Implanting surgeon: Given the fact that no adhesion barrier was used in the control group, it was impossible for the surgeon to be blinded to the treatment. Therefore, to avoid any bias in the conduct of the surgical procedure, randomization took place during the primary procedure only after colorectal carcinoma resection and prior to formation of the temporary loop ileostomy.

Medical Records: All medical records (source documents) documenting the adhesion barrier application procedure through hospital discharge and all follow-ups were not blinded, because the operation record didn’t indicate whether the anti-adhesion product was applied.

Central reviewers: The image data in the Phase 2 operation were submitted to the site reviewers for evaluation to determine the primary endpoints and secondary endpoints, who remained blinded throughout the study.

Monitors: Monitors were not blinded because the detachable labels provided with the product identified the product and might be used in the study device accountability records and patient research file for the purpose of device accountability and source document validation.

1.3.3 Sample Size

The relevant literature review revealed observed percentages of subjects with pelvic wall adhesions of 41% and 49.3% for INTERCEED™ and of 76% for Control [1,2]. Therefore, for the sample size determination, the assumption was conservatively made that the proportions of subjects with adhesions in INTERCEED™ and Control groups would be 0.5 and 0.75, respectively. With a one-sided significance level of 0.025, a sample size of 77 subjects in INTERCEED™ group and 77 subjects in Control group were required to achieve 90% power to detect a difference of 0.25 between the two group proportions using a one-sided Chi-square test. In order to adjust for a 30% dropout rate, a total of 110 subjects in INTERCEED™ group and 110 subjects in Control group, for a total of 220 subjects, were enrolled.

2 Basic Principles for Statistical Analysis

2.1 General Rules

Statistical analysis will be performed using SAS 9.4 or higher version statistical software. The two-sided 95% confidence interval for the proportion of subjects free of adhesions in the treatment groups will be provided by the Clopper-Pearson method. In addition, the two-sided Wald 95% confidence interval for the difference of two independent proportions (experimental group minus control group) will be constructed and used to test the null hypothesis for the superiority. If the lower limit of the confidence interval is greater than 0, it can be concluded that the experimental group is superior to the control group. Descriptive statistics will be adopted for statistical analysis, and the continuous variables will be summarized using the number of cases, mean, standard deviation, median, quartiles, maximum, and minimum; the categorical variables will be summarized using the missing value, number of cases, and percent. Unless otherwise specified, the number of subjects without missing data in the analysis set selected will be used as the denominator for percent calculation. Table 2 describes the numbers of decimal places kept for the statistical parameters.

Table 2 Number of Decimal Places Reserved for the Statistical Parameters

Statistics	Number of Decimal Places Reserved
Mean, median	Keep one more decimal place than the source data, but not more than 3 decimal places
Standard deviation, 95% confidence interval	Keep two more decimal places than the source data, but not more than 3 decimal places
Maximum, minimum	Keep the same decimal place as the source data, but not more than 3 decimal places
Percent	Keep one decimal place, express the percent as “100” if it reaches a hundred percent, and express it as “0” if it is 0

P value	Keep three decimal places, and express it as P < 0.001 when all the first three decimal places are 0

2.2 Definition of Analysis Sets

The 3 analysis sets in this study are defined as follows:

- The Intent to Treat (ITT) analysis set will include all randomized patients.
- The Per Protocol (PP) analysis set will include subjects in the ITT analysis set who did not have may major protocol deviations that have a serious impact on the effectiveness and safety in patients.
- The Safety (SS) analysis set will include all subjects who have been actually treated with the study device.

The ITT and PP analysis sets should be used to analyze the primary effectiveness endpoint and secondary effectiveness endpoints. However, the primary analyses will be based on the ITT analysis set. PP analysis will be regarded as supportive analysis.

The SS analysis set will be used to analyze the safety endpoints.

2.3 Data Processing Principles

2.3.1 Definition of Baseline

In this study, baseline is defined as the results of the last non-missing investigations before the phase 1 operation.

2.3.2 Definition of Study Days

Not applicable.

2.3.3 Definition of End of Study Day

A subject completes the study after completing Visit 6 or Visit 7 specified in the protocol. The study ends when the last subject completes the last visit or withdraws from the study prematurely.

2.3.4 Definition of Analysis Window

The analyses performed over time will be performed based on the visits directly collected among the data and thereby the analysis window is not applicable. Only the results of scheduled visits will be summarized in the form of tabulation, and the contents of unscheduled visits will be listed only.

2.3.5 Handling of Missing Data

For the primary endpoint (presence or absence of adhesions), no imputation will be made for missing data during primary analyses. However, during the sensitivity analysis, the missing primary endpoint will be imputed by the Multiple Imputation (MI) method. When developing MI model, the following baseline variables and the variables for phase 1 operation will be used, including the subject's age, gender, randomized adhesion barrier product used during phase 1

operation, presence or absence of adhesions during phase 1 operation, duration of phase 1 operation, blood loss and incision length, and radiotherapy or chemotherapy used at baseline or not.

The secondary endpoint will be analyzed based on the ITT set. No imputation will be made for missing data. All secondary study endpoints will be analyzed using available data.

2.4 Multiplicity Adjustment

Not applicable.

2.5 Subgroup Analyses

In this study, appropriate subgroup analyses will be performed as needed.

Subgroup analysis of the primary endpoint: neoadjuvant radiotherapy (present/absent), study site.

2.6 Pooling of Study Sites

The data of all sites will be pooled and analyzed together.

3 Statistical analysis

3.1 General Information of Subjects

3.1.1 Subjects Disposition

Screened subjects and screen-failure subjects and the reasons for screen failure will be separately described using the number of cases (percentage). Meanwhile, the disposition of randomized subjects in each treatment group and total will be summarized per site. The ITT, PP, and SS analysis sets will be descriptively summarized using the same method.

For all subjects enrolled, the number and percentage of subjects who complete the trial and those who prematurely withdraw from the study will be separately calculated, wherein completion of trial is defined as: a subject completes the study after completing Visit 6 or Visit 7 specified in the protocol. For subjects who withdraw from the study prematurely, the main reasons for withdrawal are classified as: withdrawal of consent, doctor's judgment, adverse event, subject death, loss to follow-up, termination by health authority, sponsor or investigator, and other reasons. The number and percentage of subjects will be calculated for each of the causality categories above.

Subjects' study completion profile and distribution in the analysis sets will be tabulated.

3.1.2 Protocol Deviations

In order to evaluate whether the protocol is implemented as required, before the database is locked, all protocol deviations will be identified based on the data content and protocol requirements, major protocol deviations and whether or not they are included in the PP analysis set will be summarized and described per type, and the number and percentage of subjects with protocol deviation will be calculated. All the major protocol deviations will be tabulated.

3.1.3 Demographics and Baseline Characteristics

The demographics and baseline characteristics will be described per treatment group and in total using the ITT analysis set. The categorical variables, including the gender (male, female), ethnicity (Asian, others), nation (Han, others), preoperative neoadjuvant chemotherapy (yes, no), etc., will be summarized using the missing value, number of cases, and percentage. The continuous variables, including the age, body height, and body weight, etc., will be summarized using the number of cases, missing value, mean, standard deviation, median, quartiles, maximum, and minimum.

For categorical variables, the missing values will not be included in the denominator for percent calculation.

3.1.4 Medical History

The medical history includes the pre-existing conditions and surgical history (including the surgical history within 14 days prior to phase 1 operation, from phase 1 operation to before phase 2 operation, and from end of phase 2 operation to 6-7 months after phase 1 operation). This analysis will be based on the SS analysis set, the pre-existing conditions and surgical history will be coded per treatment group and overall profile using the MedDRA 23.1 coding dictionary. And the medical history will be summarized per System Organ Class (SOC) and Preferred Term (PT) using the number of cases (percentage).

In addition, all information related to the medical history will be tabulated.

3.1.5 Prior Medications, Concomitant Medications, and Concomitant Therapies

Prior medication is defined as any drug used before phase 1 operation (i.e., the medication end date occurs before phase 1 operation).

Concomitant medication is defined as any drug that is used after phase 1 operation (i.e., the medication start date occurs after phase 1 operation) or that has been used before phase 1 operation but continues to be used after phase 1 operation.

The prior medications and concomitant medications will be summarized based on the SS analysis set.

Besides, the prior medications and concomitant medications will be coded according to the WHODRUG dictionary (GLOBAL B3 September 1, 2020) and summarize by frequency and percentage according to the therapeutic classification (ATC 2) and chemical classification (ATC 4).

If the concomitant medication start date is partially missing, the information in Table 3 will be used to determine whether the medication is a concomitant medication.

Table 3 Handling of Missing Date

Known information	Missing information	Prior medication or not
[None]	Year, month, day	Yes
Month, day	Year	Yes
Year	Month, day	Yes, if year ≥ year of the first hospital admission
Year, month	Day	Yes, if year = year of the first hospital admission, and month ≥ month of the first hospital admission
Year, day	Month	Yes, if year ≥ year of the first hospital admission

In addition, the details on each subject's prior medications, concomitant medications, preoperative radiotherapy, chemotherapy, and concomitant therapies will be tabulated.

3.2 Surgical Data and Product Use Profile

3.2.1 Surgical Data

The surgical data of phase 1 operation will be descriptively summarized based on the SS analysis set.

The variables, including whether or not adhesions are observed during operation (yes, no), site of adhesions (four abdominal quadrants), extent and severity (Grades 1, 2, 3) of adhesions, whether the adhesions are treated or not (yes, no), and closure of target incision (use of absorbable suture to suture the target incision, others), will be summarized using the number of cases (percentage). Other variables, including the duration of operation, blood loss, number of sterile gloves used, length of target incision, etc., will be summarized using the number of cases, mean, standard deviation, median, quartiles, maximum, and minimum.

3.2.2 Product Use

The product use profile in the experimental group will be tabulated based on the SS analysis set.

3.3 Effectiveness Endpoints Analysis

3.3.1 Primary Effectiveness Endpoint Analysis

The primary effectiveness endpoint is the proportion of subjects free of incision adhesions at the main target incision site observed in the two groups (experimental group and control group). The ITT and PP analysis sets will be used to analyze the primary effectiveness endpoint. The ITT analysis will be regarded as the primary analysis, and PP analysis as supportive analysis.

The statistical hypotheses for the primary endpoint are as follows:

- H_0: $P_I \leq P_C$
- H_a: $P_I > P_C$

Where P_I is the proportion of subjects free of adhesions in the experimental group, and P_C is the proportion of subjects free of adhesions in the control group.

The proportion of subjects free of adhesions in each treatment group will be summarized and calculated as: number of subjects free of adhesions divided by the total number of subjects randomized to receive the treatment. The two-sided 95% confidence interval for the proportion of subjects free of adhesions in the treatment groups will be provided by the Clopper-Pearson method. In addition, the two-sided Wald 95% confidence interval for the difference of two independent proportions (experimental group minus control group) will be constructed and used to test the null hypothesis for the superiority. If the lower limit of the confidence interval is greater than 0, it can be concluded that the experimental group is superior to the control group.

```
proc freq data =data;
        weight count;
        tables group*outcome / riskdiff(CL=WALD);
run;
```

Furthermore, a sensitivity analysis for the primary endpoint will be added. The stratification factor “presence or absence of neoadjuvant radiotherapy” will be adjusted to estimate the rate difference of the two groups and corresponding 95% CI.

3.3.2 Secondary Effectiveness Endpoint Analysis

The secondary effectiveness endpoints will be summarized based on the SS analysis set.

The incidence of mechanical ileus in subjects will be descriptively summarized per treatment group using the number of cases (percentage). The incidence of ileus will be compared between groups using the chi-square test, with the P-value calculated. The two-sided 95% confidence interval for the proportion of subjects with mechanical ileus in the treatment groups will be provided by the Clopper-Pearson method. In addition, the two-sided Wald 95% confidence interval for the difference of two independent proportions (experimental group minus control group) will be constructed.

The extent (no adhesions, grades 1, 2, 3) and severity (no adhesions, grades 1, 2, 3) of adhesions at the target surgical incision site and four abdominal quadrants observed during the phase 2 operation will be descriptively summarized per treatment group using the number of cases (percentage).

In addition, the extent and severity of adhesions at the target incision will be compared between groups using MH (Mantel - Haenszel) chi-square test, with the P-value calculated.

```
proc freq data=data;
    tables treat*response / chisq cmh nocol nopct;
    weight count;
run;
```

3.4 Safety Analysis

All safety analyses will be based on the SS analysis set. A summary will be made per treatment group, and treatment grouping will be made according to subject's actual treatment. The safety analyses include:

- Incidence of surgical site infection (SSI) at the target incision after the phase 1 operation;
- Incidence of full-thickness disruption of target incision after the phase 1 operation;
- Incidence of wound healing delayed event at the target incision after the phase 1 operation;
- Adverse events
- Physical examination

The incidences of SSI/full-thickness disruption/wound healing delayed event at the target incision after the phase 1 operation will be descriptively summarized using the number of cases (percentage), and the 95% CI for each event will be provided per treatment group using the Clopper-Pearson method; in addition, the two-sided Wald 95% confidence interval for the difference in proportion of subjects of each event between treatment groups (experimental group minus control group) will be constructed.

3.4.1 Adverse events

All adverse events (AEs) will be summarized, and the AEs will be coded using the MedDRA 23.1 dictionary.

An adverse event refers to any detrimental medical events in the course of a clinical trial, whether or not related to the investigational medical device. All AEs, study device failure, and other product problems must be documented in the medical record since the signing of informed consent. In the meantime, for non-serious AEs (excluding ileus-related events) that occur during the period from 30 days after the phase 1 operation to the second hospital admission before the phase 2 operation specified in the protocol, or between Visit 6 and Visit 7, recording and collection are not required if they are assessed as not related or unlikely related to the study device by the study doctor.

The incidences of AEs will be summarized per treatment group and in total using the number of cases (percentage). During the summary of number of cases per PT, if a subject experienced the same AE (distinguished per PT) repeatedly, he/she will be counted once only when calculating the number of cases; During the summary per severity of AE, for the same AE of different severity, the most severe one will be counted when calculating the number of cases.

According to the rules above, the AEs will be summarized generally and per SOC and PT level, and the types of AEs are summarized as follows:

- All AEs recorded during the study period in the EDC
- AEs related to the study product/phase 1 operation/phase 2 operation (including: definitely related, probably related, possibly related, and unlikely related)
- SAE
- Serious AEs related to the study product/phase 1 operation/phase 2 operation (including: definitely related, probably related, possibly related, and unlikely related)

In addition, for AEs that have occurred at least once, the number of cases and percentage will be calculated per SOC, PT, and severity (mild, moderate, and severe), and the same analysis will also be performed for AEs related to the study product.

All AEs will be tabulated to record the AE name (PT), onset date, end date, severity of AE, SAE or not, classification of SAE, relevance with the study product, action taken, and outcome, etc., and the AEs/SAEs leading to death will be tabulated independently.

3.4.2 Physical examination

The physical examination data will be collected at baseline and at each scheduled visit after baseline, and the results will be evaluated as “Normal”, “Abnormal, not clinically significant”, or “Abnormal, clinically significant”. The physical examination results of each scheduled visit will be summarized per treatment group and overall profile, for which the number of cases and percentage under each category of the results will be calculated and cross tabulations will be formulated. The abnormal records will be listed.

3.5 Analysis of Other Endpoints

3.5.1 Study Product Defects

The study product defects will be tabulated.

4 Interim Analysis and Data Monitoring Committee (DMC)

Based on the feedback from the investigator that the target incision adhesion rate observed during the phase 2 operation (ileostomy reversal) is very low, an interim analysis will be added. The interim analysis will be performed after at least 94 subjects (accounting for at least 61% of the total subjects) have completed the primary endpoint evaluation.

The timeline for the interim analysis is September 15, 2020.

The interim analysis will include the following subjects:

a) All subjects that have undergone the phase 2 operation,

b) Subjects who withdrew from the study without undergoing the phase 2 operation;

c) Subjects who have neither undergone the phase 2 operation nor withdrawn from the study, but have undergone the phase 1 operation before or on September 15, 2019.

The conditional power (CP) is the probability that the final result will be significant, given the data observed as of the interim analysis. The equation for calculating the CP is as follows:

$$P_{lk}(\theta) = \Phi\left(\frac{-Z_k\sqrt{I_k} - z_{1-\alpha}\sqrt{I_k} - \theta(I_K - I_k)}{\sqrt{I_K - I_k}}\right)$$

Where,

$Z_k = \frac{p_{2k}-p_{1k}}{\sqrt{\sigma^2\left(\frac{1}{n_{1k}}+\frac{1}{n_{2k}}\right)}}$; p_{2k} and p_{1k} are the adhesion rates of the experimental group and control group at the time of the interim analysis, while n_{2k} and n_{1k} are the numbers of subjects with evaluable primary endpoint in the experimental group and control group at the time of the interim analysis.

$$I_k = \frac{1}{\sigma^2}\left(\frac{1}{n_{1k}} + \frac{1}{n_{2k}}\right)^{-1}$$

$I_K = \frac{1}{\sigma^2}\left(\frac{1}{n_1} + \frac{1}{n_2}\right)^{-1}$, n is the total number of subjects in the experimental group and control group, and in this study, $n_1 = n_2 = 77$;

$\sigma^2 = \bar{p}(1-\bar{p}), \bar{p} = (P_1+P_2)/2$, P_2 and P_1 are the expected adhesion rates of the experimental group and control group, and in this study, $P_2=0.5$, $P_1=0.75$);

$\Theta = P_2 - P_1$;

$Z_{1-\alpha} = Z_{1-0.025} = 1.96$ (one-sided 97.5% critical Z-value);

Φ: Area under the standard normal distribution curve

Table4 provides the CP for various adhesion rate differences between INTERCEED group and control group at the time of the interim analysis. Given an anticipated dropout rate of 30%, it is planned that there will be a total of 154 subjects with evaluable primary endpoint (77 in each group) by the time the study is completed. The interim analysis will be performed after at least 94 subjects (accounting for at least 61% of the total subjects) have completed the primary endpoint evaluation. If CP ≤ 60%, the observed target incision adhesion rate difference between the two groups is only 0.10 or so, which is much smaller than the assumed difference of 0.25 used in the sample size calculation. Accordingly, the study will be terminated due to the low adhesion rate and the small effect size between INTERCEED group and control group. Otherwise, the study will continue until it is completed as originally planned.

Database lock will be performed for the interim analysis. All data provided for analysis will be cleaned through 100% source data verification. Statistical analyses will be performed according to the updated and approved protocol and SAP to determine whether the interim results meet the predefined threshold for early discontinuation (CP ≤ 60%).

Table4 Conditional Power for the Effect Size between Treatment Groups Observed during the Interim Analysis

Adhesion Rate Difference between Treatment Groups Observed at the Interim Analysis	Available Data at Interim Analysis Percentage of Subjects with Evaluable Primary Endpoint (Number of Subjects)				
	61% (94)	66% (102)	70% (108)	72% (112)	75% (116)
-0.02	0.19	0.11	0.07	0.04	0.02
-0.06	0.35	0.26	0.2	0.16	0.12
-0.08	0.45	0.37	0.3	0.26	0.21
-0.1	0.55	0.48	0.42	0.38	0.34
-0.11	0.59	0.54	0.49	0.45	0.41
-0.12	0.64	0.6	0.56	0.52	0.49
-0.13	0.69	0.65	0.62	0.6	0.57
-0.14	0.73	0.7	0.68	0.66	0.64
-0.15	0.77	0.75	0.74	0.72	0.71
-0.16	0.81	0.8	0.79	0.78	0.78
-0.18	0.87	0.87	0.87	0.87	0.87

5 Modifications to the Original Analysis Plan

Not applicable.

6 References

1. Sekiba K. Use of Interceed(TC7) absorbable adhesion barrier to reduce postoperative adhesion reformation in infertility and endometriosis surgery. The Obstetrics and Gynecology Adhesion Prevention Committee. Obstet Gynecol. 1992 Apr;79(4):518-22.
2. Azziz R. Microsurgery alone or with INTERCEED Absorbable Adhesion Barrier for pelvic sidewall adhesion re-formation. The INTERCEED (TC7) Adhesion Barrier Study Group II. Surg Gynecol Obstet. 1993 Aug;177(2):135-9.

7 Appendixes

7.1 Four Abdominal Quadrants (Figure)