Clinical trial results:
A Prospective, Controlled, Randomized, Multi-Center, Exploratory Pilot Study Evaluating the Safety and Potential Trends in Efficacy of Adhexil™

Summary

EudraCT number	2007-001326-26
Trial protocol	DE GB ES
Global end of trial date	29 August 2008

Results information

Result version number	v1 (current)
This version publication date	01 January 2023
First version publication date	01 January 2023

Trial information

Trial identification

Sponsor protocol code	AA-GYN-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00544310
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OMRIX Biopharmaceuticals Ltd
Sponsor organisation address	MDA Blood Bank, Sheba Hospital, Ramat Gan POB 888, Kiryat Ono, Israel, 55000
Public contact	Patricia Schleckser, Ethicon Inc, pschleck@its.jnj.com
Scientific contact	Richard Kocharian, MD, PhD, Ethicon Inc, rkochar1@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 February 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 July 2008
Global end of trial reached?	Yes
Global end of trial date	29 August 2008
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to evaluate the safety and initial efficacy of the anti-adhesion kit (AA) AdhexilTM for the prevention and/or reduction of post-operative adhesions in patients who are undergoing a surgical procedure involving the ovaries.

Protection of trial subjects:

Prior to study participation, the procedures and any known or likely risks were explained to the subject by the investigator or other medically qualified co-investigator. An informed consent form was provided containing all the required information. Any questions were answered and the subject was then given sufficient time to consider their participation in the study before signing the consent form.

The investigator (or designee) explained to subjects that they were completely free to refuse to enter the study, or to withdraw from it at any time, without any consequences for their further care and without the need to justify their decision.

Subjects were made aware that all information would be treated confidentially, and they would be identified by a study code.

Background therapy:

In both the US and EU, several products are marketed for reduction of post-operative adhesions but all have limitations. An ideal adhesion barrier should be non reactive, but protect tissue at risk during the critical wound healing period before being absorbed and cleared, it should remain adherent to the target tissue even in the presence of bleeding and it should be easy to apply during laparoscopic procedures performed on adhesiogenic organs such as ovaries and adnexa.

The potential of a variety of materials to reduce the occurrence and severity of adhesion formation has been investigated. This has included agents that affect adhesion formation at various levels, such as fibrinolytic agents, anti inflammatory, antibiotics and mechanical barriers (films, gels and liquids absorbable and non-absorbable). Many of the products developed have been difficult to use in open surgery, and particularly in laparoscopic settings.

Adhexil™ anti-adhesion kit consists of the components required to form a protective fibrin polymer together with an application device. The components that form the fibrin polymer, Biological Active Component (BAC) and Thrombin, are human blood derivatives.

Evidence for comparator:

There was no active comparator used in this study. All subjects had their 1st ovary treated with Adhexil and compared to the 2nd ovary which did not receive any treatment.

Actual start date of recruitment	23 October 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Germany: 10
Worldwide total number of subjects	17
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First Subject Enrolled: 23-Oct-07; Last Subject Enrolled: 16-Jul-08, Completed: 29-Aug-08. Each subject enrolled had one ovary treated with Adhexil and other ovary untreated. Thus 17 enrolled subjects resulted in 34 evaluable (17 treated & 17 untreated) ovaries. One subject withdrew after completing index procedure resulting in 32 evaluable ovaries

Pre-assignment

Screening details:

Prospective subjects were screened within 21 days prior to surgery. Prior to any study related procedures, subjects were fully informed of all aspects of the study and asked to sign a consent form.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Subject, Assessor

Blinding implementation details:

Due to the nature of the investigational product in this study, it was not possible for the surgeon to be blinded to treatment. The subject was blinded to treatment received. To avoid any bias in the assessment of incidence, extent and severity of adhesions, both 1st Look Laparoscopy (1LL) and 2nd Look Laparoscopy (2LL) surgeries were recorded on DVD and evaluated by a blinded independent surgeon. The proficiency of Adhexil application was also evaluated by a blinded reviewer.

Arms

Are arms mutually exclusive?	No
Arm title	Treated Ovary (1st Look Laparoscopy)

Arm description:

Undergoing elective laparoscopic surgery due to known or suspected bilateral ovarian disease were enrolled and underwent the index study surgical procedure, referred to as the 1st Look Laparoscopy (1LL).

Arm type	Experimental
Investigational medicinal product name	Adhexil™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implantation matrix
Routes of administration	Implantation

Dosage and administration details:

The amount of Adhexil™ required depended upon the area and location of the site to be treated. Adhexil™ was to be applied so that it extended 1-2 cm beyond the margins of the raw surface. The remaining volume of the kit was then to be applied to the entire assigned ovary and the raw surfaces of adjacent structures at the surgeon’s discretion. It was intended that in most cases, the maximum of 10 mL of Adhexil™ would be applied. Note: Adhexil treatment was applied to 1 of the 2 ovaries of each subject following a randomised assignment.

Arm title	Untreated Ovary (1st Look Laparoscopy)

Arm description:

Undergoing elective laparoscopic surgery due to known or suspected bilateral ovarian disease enrolled and underwent the index study surgical procedure, referred to as the 1st Look Laparoscopy (1LL).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treated Ovary (2nd Look Laparoscopy)

Arm description:

Subjects were to undergo a second look laparoscopy (2LL), 6 (+/- 4) weeks following first laparoscopy if

considered beneficial because of the probability of formation of new adhesions.

Arm type	Experimental
Investigational medicinal product name	Adhexil™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implantation matrix
Routes of administration	Implantation

Dosage and administration details:

The amount of Adhexil™ required depended upon the area and location of the site to be treated. Adhexil™ was to be applied so that it extended 1-2 cm beyond the margins of the raw surface. The remaining volume of the kit was then to be applied to the entire assigned ovary and the raw surfaces of adjacent structures at the surgeon's discretion. It was intended that in most cases, the maximum of 10 mL of Adhexil™ would be applied. Note: Adhexil treatment was applied to 1 of the 2 ovaries of each subject following a randomised assignment.

Arm title	Untreated Ovary (2nd Look Laparoscopy)

Arm description:

Subjects were to undergo a second look laparoscopy (2LL), 6 (+/- 4) weeks following first laparoscopy if considered beneficial because of the probability of formation of new adhesions.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Due to the nature of the investigational product in this study, it was not possible for the surgeon to be blinded to treatment. The subject was blinded to treatment received. To avoid any bias in the assessment of incidence, extent and severity of adhesions, both 1st Look Laparoscopy (1LL) and 2nd Look Laparoscopy (2LL) surgeries were recorded on DVD and evaluated by a blinded independent surgeon. The proficiency of Adhexil application was also evaluated by a blinded reviewer.

Number of subjects in period 1	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)
Started	17	17	16
Completed	17	17	16

Number of subjects in period 1	Untreated Ovary (2nd Look Laparoscopy)
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	17	17	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	29.2		
full range (min-max)	22 to 40	-	
Gender categorical Units: Subjects			
Female	17	17	
Diagnosis of Ovarian Disease			
The subjects' diagnoses of ovarian disease are summarised.			
Units: Subjects			
Endometriosis	8	8	
Teratoma / bilateral teratoma	3	3	
Endometriosis and teratoma	1	1	
Endometriosis and ovarian cyst	3	3	
Endometrial cyst	1	1	
Adhesion and ovarian cyst	1	1	
Race Units: Subjects			
Caucasian	17	17	
Ethnicity Units: Subjects			
Hispanic/Latino	9	9	
Northern European	8	8	

Subject analysis sets

Subject analysis set title	1st Look Laparoscopy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Seventeen (17) subjects were enrolled and underwent the index study surgical procedure, referred to as the 1st Look Laparoscopy (ILL). Each subject had 1 ovary treated with Adhexil™ and 1 ovary left untreated. In this subject analysis set there are a total of 34 [(17 (treated) +17 - (untreated)] evaluable ovaries.

Subject analysis set title	2nd Look Laparoscopy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

A total of 16/17 subjects completed 2nd Look Laparoscopy, 6 (+/- 4) weeks following first laparoscopy if considered beneficial because of the probability of formation of new adhesions.. Each subject had 1 ovary treated with Adhexil™ and 1 ovary left untreated. In this subject analysis set there are a total of 32 [16 (treated) +16 (untreated)] evaluable ovaries.

Note: 1 subject withdrew consent after completing the index procedure.

Reporting group values	1st Look Laparoscopy	2nd Look Laparoscopy	
Number of subjects	17	16	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	17	16	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	29.2		
full range (min-max)	22 to 40		
Gender categorical Units: Subjects			
Female	17	16	
Diagnosis of Ovarian Disease			
The subjects' diagnoses of ovarian disease are summarised.			
Units: Subjects			
Endometriosis	8	7	
Teratoma / bilateral teratoma	3	3	
Endometriosis and teratoma	1	1	
Endometriosis and ovarian cyst	3	3	
Endometrial cyst	1	1	
Adhesion and ovarian cyst	1	1	
Race Units: Subjects			
Caucasian	17	16	
Ethnicity Units: Subjects			
Hispanic/Latino	9	8	
Northern European	8	8	

End points

End points reporting groups

Reporting group title	Treated Ovary (1st Look Laparoscopy)

Reporting group description:

Undergoing elective laparoscopic surgery due to known or suspected bilateral ovarian disease were enrolled and underwent the index study surgical procedure, referred to as the 1st Look Laparoscopy (1LL).

Reporting group title	Untreated Ovary (1st Look Laparoscopy)

Reporting group description:

Undergoing elective laparoscopic surgery due to known or suspected bilateral ovarian disease enrolled and underwent the index study surgical procedure, referred to as the 1st Look Laparoscopy (1LL).

Reporting group title	Treated Ovary (2nd Look Laparoscopy)

Reporting group description:

Subjects were to undergo a second look laparoscopy (2LL), 6 (+/- 4) weeks following first laparoscopy if considered beneficial because of the probability of formation of new adhesions.

Reporting group title	Untreated Ovary (2nd Look Laparoscopy)

Reporting group description:

Subjects were to undergo a second look laparoscopy (2LL), 6 (+/- 4) weeks following first laparoscopy if considered beneficial because of the probability of formation of new adhesions.

Subject analysis set title	1st Look Laparoscopy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Seventeen (17) subjects were enrolled and underwent the index study surgical procedure, referred to as the 1st Look Laparoscopy (ILL). Each subject had 1 ovary treated with Adhexil™ and 1 ovary left untreated. In this subject analysis set there are a total of 34 [(17 (treated) +17 - (untreated)] evaluable ovaries.

Subject analysis set title	2nd Look Laparoscopy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

A total of 16/17 subjects completed 2nd Look Laparoscopy, 6 (+/- 4) weeks following first laparoscopy if considered beneficial because of the probability of formation of new adhesions.. Each subject had 1 ovary treated with Adhexil™ and 1 ovary left untreated. In this subject analysis set there are a total of 32 [16 (treated) +16 (untreated)] evaluable ovaries.

Note: 1 subject withdrew consent after completing the index procedure.

Primary: Incidence of ovaries with adhesions at completion of 1st Look Laparoscopy and 2nd Look Laparoscopy

End point title	Incidence of ovaries with adhesions at completion of 1st Look Laparoscopy and 2nd Look Laparoscopy

End point description:

End point type	Primary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16[1]	16[2]
Units: Number of Adhesions				
number (not applicable)				
Absence of Adhesion	6	5	8	5
Presence of Adhesion	11	12	8	11

Notes:

[1] - 1 subject was withdrawn from the study, at the subject's request.

[2] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

Statistical analysis title	Primary Endpoint

Statistical analysis description:

The incidence of ovarian adhesions at 2LL was summarized by treatment and compared using McNemar’s Test to compare the incidence of ovaries with adhesions in Intention to Treat population. The total number of evaluable ovaries (treated and untreated) (shown as "subjects" in the table below) is 34 in 1st Look Laparoscopy and 32 in 2nd Look Laparoscopy (total of 66 observations).

Comparison groups	Untreated Ovary (1st Look Laparoscopy) v Treated Ovary (1st Look Laparoscopy) v Treated Ovary (2nd Look Laparoscopy) v Untreated Ovary (2nd Look Laparoscopy)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.1797
Method	Mcnemar

Notes:

[3] - This study was not powered to detect statistical significance. Note: The total number of ovaries (subjects) in this end point analysis (#66) corresponds to the total number of evaluable ovaries (treated and untreated) at 1st and 2nd Look Laparoscopy procedure

Secondary: Extent of Ovarian Adhesions at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point title	Extent of Ovarian Adhesions at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point description:

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16[4]	16[5]
Units: Subjects				

Overall Observations	17	17	16	16
No adhesion	6	5	8	5
<1/3 of surface with adhesions	4	4	4	3
1/3 to 2/3 of surface with adhesions	2	6	0	3
>2/3 of surface with adhesions	5	2	4	5

Notes:

[4] - 1 subject was withdrawn from the study, at the subject's request.

[5] - 1 subject was withdrawn from the study, at the subject's request.

End point values	1st Look Laparoscopy	2nd Look Laparoscopy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	32[6]		
Units: Subjects				
Overall Observations	34	32		
No adhesion	11	13		
<1/3 of surface with adhesions	8	7		
1/3 to 2/3 of surface with adhesions	8	3		
>2/3 of surface with adhesions	7	9		

Notes:

[6] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of Ovarian Adhesions at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point title	Severity of Ovarian Adhesions at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point description:

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16[7]	16[8]
Units: subjects				
Overall Observations	17	17	16	16
No adhesion	6	5	8	5
Filmy, avascular	1	0	2	1
Dense and/or vascular	1	3	1	3
Cohesive	9	9	5	7

Notes:

[7] - 1 subject was withdrawn from the study, at the subject's request.

[8] - 1 subject was withdrawn from the study, at the subject's request.

End point values	1st Look Laparoscopy	2nd Look Laparoscopy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	32[9]		
Units: subjects				
Overall Observations	34	32		
No adhesion	11	13		
Filmy, avascular	1	3		
Dense and/or vascular	4	4		
Cohesive	18	12		

Notes:

[9] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

No statistical analyses for this end point

Secondary: The American Fertility Society Scores for Adhesions of Ovaries and Tubes at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point title	The American Fertility Society Scores for Adhesions of Ovaries and Tubes at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point description:

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16[10]	16[11]
Units: Number				
arithmetic mean (standard deviation)				
Mean (SD)	10.3 (± 12.79)	10.6 (± 10.48)	7.9 (± 10.28)	11.4 (± 11.94)

Notes:

[10] - 1 subject was withdrawn from the study, at the subject's request.

[11] - 1 subject was withdrawn from the study, at the subject's request.

End point values	1st Look Laparoscopy	2nd Look Laparoscopy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	32[12]		
Units: Number				

arithmetic mean (standard deviation)				
Mean (SD)	10.4 (± 11.52)	9.6 (± 11.11)		

Notes:

[12] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

No statistical analyses for this end point

Secondary: The American Fertility Society Scores for Adhesions of Ovaries and Tubes (2nd Look Laparoscopy - 1st Look Laparoscopy)

End point title	The American Fertility Society Scores for Adhesions of Ovaries and Tubes (2nd Look Laparoscopy - 1st Look Laparoscopy)[13]

End point description:

The assessments of the overall extent and severity of adhesions as described above were used to derive American Fertility Society scores. Scores at 1st Look Laparoscopy procedure were subtracted from scores at 2nd Look Laparoscopy procedure and a difference derived in adjusted means between treatment groups.

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The AFS score at 1st Look Laparoscopy were subtracted from score at 2LL and a difference was compared between treated and untreated ovaries. Adjusted means are presented separately for treated and untreated ovaries. Summary statistics are not provided separately for 1st and 2nd Look Laparoscopy for this endpoint. Note: The table below summaries data for difference in scores between 2nd Look and 1st Look Laparoscopy, with columns presented for treated ovaries, untreated ovaries, and in total.

End point values	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)	2nd Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16[14]	16[15]	32[16]	
Units: Number				
arithmetic mean (standard deviation)				
2LL-1LL: Mean (SD)	-2.8 (± 9.70)	0.4 (± 5.21)	-1.2 (± 7.83)	

Notes:

[14] - 1 subject was withdrawn from the study, at the subject's request.

[15] - 1 subject was withdrawn from the study, at the subject's request.

[16] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

Statistical analysis title	Other Efficacy analysis

Statistical analysis description:

AFS scores was summarized by treatment at 1LL and 2LL and compared between treatments at 2LL using an analysis of covariance, with subject and treatment as factors and value at 1LL as a covariate. The difference of LS-means will be displayed as well as its 95% confidence interval and its associated p-value. The point estimate, confidence interval, and p-value shown are for the difference in adjusted means between treated and untreated ovaries with respect to difference (2LL-1LL) in AFS scores.

Comparison groups	Treated Ovary (2nd Look Laparoscopy) v Untreated Ovary (2nd Look Laparoscopy)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.2341
Method	analysis of covariance
Parameter estimate	Difference in adjusted means
Point estimate	-3.245
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.822
upper limit	2.233

Notes:

[17] - AFS Scores for Adhesions of Ovaries and Tubes (2nd Look Laparoscopy - 1st Look Laparoscopy).

Secondary: The American Fertility Society Scores for Adhesions of Ovaries Only at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point title	The American Fertility Society Scores for Adhesions of Ovaries Only at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point description:

The American Fertility Society scoring system was also used to evaluate the extent and severity of the adhesion.

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16[18]	16[19]
Units: Number				
arithmetic mean (standard deviation)				
Mean (SD)	6.4 (± 6.88)	5.6 (± 5.11)	4.6 (± 6.91)	7.1 (± 6.87)

Notes:

[18] - 1 subject was withdrawn from the study, at the subject's request.

[19] - 1 subject was withdrawn from the study, at the subject's request.

End point values	1st Look Laparoscopy	2nd Look Laparoscopy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	16[20]		
Units: Number				
arithmetic mean (standard deviation)				
Mean (SD)	6.0 (± 5.98)	5.8 (± 6.89)		

Notes:

[20] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

No statistical analyses for this end point

Secondary: The American Fertility Society Scores for Adhesions of Ovaries Only (2nd Look Laparoscopy - 1st Look Laparoscopy)

End point title	The American Fertility Society Scores for Adhesions of Ovaries Only (2nd Look Laparoscopy - 1st Look Laparoscopy)[21]

End point description:

The assessments of the overall extent and severity of adhesions as described above were used to derive American Fertility Society scores. Scores at 1st Look Laparoscopy procedure were subtracted from scores at 2nd Look Laparoscopy procedure and a difference derived in adjusted means between treatment groups.

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The AFS score at 1st Look Laparoscopy were subtracted from score at 2LL and a difference was compared between treated and untreated ovaries. Adjusted means are presented separately for treated and untreated ovaries. Summary statistics are not provided separately for 1st and 2nd Look Laparoscopy for this endpoint. Note: The table below summaries data for difference in scores between 2nd Look and 1st Look Laparoscopy, with columns presented for treated ovaries, untreated ovaries, and in total.

End point values	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)	2nd Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16[22]	16[23]	32[24]	
Units: Number				
arithmetic mean (standard deviation)				
2LL - 1LL: Mean (SD)	-1.9 (± 6.49)	1.3 (± 4.30)	-0.3 (± 5.66)	

Notes:

[22] - 1 subject was withdrawn from the study, at the subject's request.

[23] - 1 subject was withdrawn from the study, at the subject's request.

[24] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

Statistical analysis title	Other Efficacy Endpoints

Statistical analysis description:

The American Fertility Society Scores for Adhesions of Ovaries Only at 1st Look Laparoscopy and 2nd Look Laparoscopy procedures

Comparison groups	Treated Ovary (2nd Look Laparoscopy) v Untreated Ovary (2nd Look Laparoscopy)

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1125
Method	Analysis of covariance
Parameter estimate	Difference in adjusted means
Point estimate	-3.049
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.904
upper limit	0.805

Secondary: Incidence of Ovaries with Adhesions at 1st Look Laparoscopy

End point title	Incidence of Ovaries with Adhesions at 1st Look Laparoscopy[25]

End point description:

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st laparoscopic (index) procedure.

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms since it records the data for 1st Look Laparoscopy only.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	1st Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	17	17	34	
Units: subjects				
No adhesion	6	5	11	
Not categorized adhesion	11	12	23	
Total	17	17	34	

Statistical analyses

No statistical analyses for this end point

Secondary: Extent of Reformed Ovarian Adhesions at 2nd Look Laparoscopy

End point title	Extent of Reformed Ovarian Adhesions at 2nd Look Laparoscopy[26]

End point description:

Secondary Assessment of Efficacy Endpoint
If an adhesion was also present (at the same site) at 1st Look Laparoscopy then the 2nd Look

Laparoscopy adhesion will be considered as a reformed adhesion. If at 1st Look Laparoscopy, surgery was performed (other than adhesiolysis) at that site then the reformed adhesion is categorized as "2b". If no surgery (other than adhesiolysis) was performed at that site then the reformed adhesion is categorized as "2a".

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 2nd Look Laparoscopy procedure, 6 (+/- 4) weeks following the index procedure, in subjects who had at least one ovary with an adhesion at 1st Look Laparoscopy.

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: the extent of reformed ovarian adhesions at 2nd Look Laparoscopy in subjects who had at least one ovary with an adhesion at 1st Look Laparoscopy. The end point is not reporting statistics for all the arms since it records the data for 2nd Look Laparoscopy.

End point values	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)	2nd Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16[27]	16[28]	32[29]	
Units: Adhesions				
Overall Observations	12	12	24	
No reformed adhesions	6	3	9	
<1/3 of surface with adhesions	2	2	4	
Reformed 2a	2	1	3	
Reformed 2b	0	1	1	
1/3 to 2/3 of surface with adhesions	0	2	2	
Reformed 2a (1/3 to 2/3)	0	2	2	
Reformed 2b (1/3 to 2/3)	0	0	0	
>2/3 of surface with adhesions	4	5	9	
Reformed 2a (>2/3)	4	3	7	
Reformed 2b (>2/3)	0	2	2	

Notes:

[27] - 1 subject was withdrawn from the study, at the subject's request.

[28] - 1 subject was withdrawn from the study, at the subject's request.

[29] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

Statistical analysis title	Other Efficacy Endpoints

Statistical analysis description:

Comparison between the extent of reformed adhesions in treated and untreated ovaries using the Wilcoxon signed rank test gave a p-value of 0.3750. Extent of Reformed Ovarian Adhesions at the extent of reformed ovarian adhesions at 2nd Look Laparoscopy, 6 (+/- 4) weeks following the index procedure in subjects who had at least one ovary with an adhesion at 1st Look Laparoscopy (index procedure).

Comparison groups	Treated Ovary (2nd Look Laparoscopy) v Untreated Ovary (2nd Look Laparoscopy)

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.375
Method	Wilcoxon signed rank test

Secondary: Extent of de novo Ovarian Adhesions at 1st Look Laparoscopy

End point title	Extent of de novo Ovarian Adhesions at 1st Look

End point description:

If an adhesion was not present (at the same site) at 1LL, the 2LL adhesion will be considered as a de novo adhesion. If at 1LL, surgery was performed at that site then the de novo adhesion is categorized as "1b". If no surgery was performed then the de novo adhesion is categorized as "1a".

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st Look Laparoscopic (index) procedure.

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point is not reporting statistics for all arms since it records the extent of de novo ovarian adhesions in subjects who had at least one ovary without an adhesion at 1st Look Laparoscopy.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	1st Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	17	17	34	
Units: Ovaries				
Overall Observations	7	7	14	
No de novo adhesions	5	5	10	
<1/3 of surface with adhesions	2	1	3	
De novo 1a (<1/3)	2	1	3	
De novo 1b (<1/3)	0	0	0	
1/3 to 2/3 of surface with adhesions	0	1	1	
De novo 1a (1/3 to 2/3)	0	1	1	
De novo 1b (1/3 to 2/3)	0	0	0	
>2/3 of surface with adhesions	0	0	0	
De novo 1a (>2/3)	0	0	0	
De novo 1b (>2/3)	0	0	0	

Statistical analyses

Statistical analysis title	Extent of de novo Ovarian Adhesions

Statistical analysis description:

Extent of de novo Ovarian Adhesions

Comparison groups	Treated Ovary (1st Look Laparoscopy) v Untreated Ovary (1st Look Laparoscopy)

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.375
Method	Wilcoxon signed rank test

Secondary: Incidence of Ovaries with Reformed or de novo Adhesions at 2nd Look Laparoscopy

End point title	Incidence of Ovaries with Reformed or de novo Adhesions at 2nd Look Laparoscopy[31]

End point description:

If an adhesion was also present (at the same site) at 1st Look Laparoscopy then the 2nd Look Laparoscopy adhesion will be considered as a reformed adhesion. If at 1st Look Laparoscopy, surgery was performed (other than adhesiolysis) at that site then the reformed adhesion is categorized as "2b". If no surgery (other than adhesiolysis) was performed at that site then the reformed adhesion is categorized as "2a".

If an adhesion was not present (at the same site) at 1st Look Laparoscopy, the 2nd Look Laparoscopy adhesion will be considered as a de novo adhesion. If at 1st Look Laparoscopy, surgery was performed at that site then the de novo adhesion is categorized as "1b". If no surgery was performed then the de novo adhesion is categorized as "1a".

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The incidence of ovaries with reformed or de novo adhesions at 2nd Look Laparoscopy is summarised. This end point is not reporting statistics for all the arms since it records the data for 2nd Look Laparoscopy only.

End point values	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)	2nd Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16[32]	16[33]	32[34]	
Units: Subjects				
No adhesion	8	5	13	
De novo a1	2	2	4	
Reformed 2a	6	6	12	
Reformed 2b	0	3	3	
Total	16	16	32	

Notes:

[32] - 1 subject was withdrawn from the study, at the subject's request.

[33] - 1 subject was withdrawn from the study, at the subject's request.

[34] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of Reformed Ovarian Adhesions at 2nd Look Laparoscopy

End point title	Severity of Reformed Ovarian Adhesions at 2nd Look Laparoscopy[35]

End point description:

End point type	Secondary

End point timeframe:

The extent of reformed ovarian adhesions assessment after completion of 2nd Look Laparoscopic procedure, 6 (+/- 4) weeks following the index procedure, in subjects who had at least one ovary with an adhesion at 1st Look Laparoscopy (index procedure).

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The severity of reformed ovarian adhesions in subjects who had at least one ovary with an adhesion at 1st Look Laparoscopy is summarized and comparison between the severity of reformed adhesions in treated and untreated ovaries was made.

End point values	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)	2nd Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16[36]	16[37]	32[38]	
Units: Adhesion				
Overall Observations	12	12	24	
No reformed adhesions	6	3	9	
Filmy, avascular	1	0	1	
Reformed 2a (Filmy, avascular)	1	0	1	
Reformed 2b (Filmy, avascular)	0	0	0	
Dense and/or vascular	1	2	3	
Reformed 2a (Dense and/or vascular)	1	2	3	
Reformed 2b (Dense and/or vascular)	0	0	0	
Cohesive	4	7	11	
Reformed 2a (Cohesive)	4	4	8	
Reformed 2b (Cohesive)	0	3	3	

Notes:

[36] - 1 subject was withdrawn from the study, at the subject's request.

[37] - 1 subject was withdrawn from the study, at the subject's request.

[38] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

Statistical analysis title	Other Efficacy Analysis

Statistical analysis description:

Severity of Reformed Ovarian Adhesions

Comparison groups	Untreated Ovary (2nd Look Laparoscopy) v Treated Ovary (2nd Look Laparoscopy)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3438
Method	Wilcoxon signed rank test

Secondary: Severity of de novo Ovarian Adhesions at 1st Look Laparoscopy

End point title	Severity of de novo Ovarian Adhesions at 1st Look

End point description:

If an adhesion was not present (at the same site) at 1LL, the 2LL adhesion will be considered as a de novo adhesion. If at 1LL, surgery was performed at that site then the de novo adhesion is categorized as "1b". If no surgery was performed then the de novo adhesion is categorized as "1a".

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st Look Laparoscopic (index) procedure.

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point is not reporting statistics for all arms since it records the severity of de novo ovarian adhesions in subjects who had at least one ovary without an adhesion at 1st Look Laparoscopy.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	1st Look Laparoscopy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	17	17	34	
Units: Ovaries				
Overall Observations	7	7	14	
No de novo adhesions	5	5	10	
Filmy, avascular	1	1	2	
De novo 1a (Filmy, avascular)	1	1	2	
De novo 1b (Filmy, avascular)	0	0	0	
Dense and/or vascular	0	1	1	
De novo 1a (Dense and/or vascular)	0	1	1	
De novo 1b (Dense and/or vascular)	0	0	0	
Cohesive	1	0	1	
De novo 1a (Cohesive)	1	0	1	
De novo 1b (Cohesive)	0	0	0	

Statistical analyses

Statistical analysis title	Severity of de novo Ovarian Adhesions

Statistical analysis description:

Severity of de novo Ovarian Adhesions

Comparison groups	Treated Ovary (1st Look Laparoscopy) v Untreated Ovary (1st Look Laparoscopy)
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Wilcoxon signed rank test

Secondary: Incidence of Ovarian Adhesions by Presence of Endometriosis at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point title	Incidence of Ovarian Adhesions by Presence of Endometriosis at 1st Look Laparoscopy and 2nd Look Laparoscopy

End point description:

Analysis of the incidence of adhesions in treated and untreated ovaries according to whether or not endometriosis was present at 1st look laparoscopy and again at 2nd look laparoscopy.

End point type	Secondary

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed after completion of 1st look laparoscopic (index) procedure and again after completion of 2nd look laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	Treated Ovary (1st Look Laparoscopy)	Untreated Ovary (1st Look Laparoscopy)	Treated Ovary (2nd Look Laparoscopy)	Untreated Ovary (2nd Look Laparoscopy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16[40]	16[41]
Units: Ovaries with Adhesion				
Absence of Adhesion (a)	3	3	5	4
Presence of Adhesion (a)	3	3	8	9
Absence of Endometriosis (Total)	6	6	13	13
Absence of Adhesion (b)	2	2	1	1
Presence of Adhesion (b)	8	9	2	2
Presence of Endometriosis (Total)	11	11	3	3

Notes:

[40] - 1 subject was withdrawn from the study, at subject's request.

[41] - 1 subject was withdrawn from the study, at subject's request.

End point values	1st Look Laparoscopy	2nd Look Laparoscopy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	32[42]		
Units: Ovaries with Adhesion				
Absence of Adhesion (a)	6	9		
Presence of Adhesion (a)	6	17		
Absence of Endometriosis (Total)	12	26		
Absence of Adhesion (b)	5	2		
Presence of Adhesion (b)	17	4		
Presence of Endometriosis (Total)	22	6		

Notes:

[42] - 1 subject was withdrawn from the study, at subject's request.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of Adhesions at various Anatomical Sites

End point title	Incidence of Adhesions at various Anatomical Sites

End point description:

End point type	Other pre-specified

End point timeframe:

Adhesion Assessment and Recording of Laparoscopic Examination was performed at after completion of 1st laparoscopic (index) procedure and again after completion of 2nd laparoscopic procedure, 6 (+/- 4) weeks following the index procedure.

End point values	1st Look Laparoscopy	2nd Look Laparoscopy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	16[43]		
Units: Subjects				
Anterior abdominal wall above incision site	1	0		
Anterior abdominal wall incision site	7	4		
Large bowel	12	7		
Left anterior abdominal wall	1	2		
Left anterior cul-de-sac	2	2		
Left pelvic sidewall	6	6		
Left posterior broad ligament	13	15		
Left round ligament to tube	1	4		
Left Tube	6	8		
Omentum	4	1		
Over bladder in anterior cul-de-sac	3	2		
Over uterus in anterior cul-de-sac	4	2		
Posterior cul-de-sac	7	4		
Posterior uterus	10	9		
Right anterior abdominal wall	1	1		
Right anterior cul-de-sac	1	1		
Right pelvic sidewall	9	5		
Right posterior broad ligament	13	10		
Right round ligament to tube	2	2		
Right Tube	9	8		
Small bowel	2	3		

Notes:

[43] - 1 subject was withdrawn from the study, at the subject's request.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) (serious and non serious) occurring from the date the patient signed informed consent until 30 days following the second-look control laparoscopy, was recorded.

Adverse event reporting additional description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 17 (82.35%)		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
General disorders and administration site conditions			
Feeling hot			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Impaired healing			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 17 (41.18%)		
occurrences (all)	7		
Nausea			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Toothache			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Vulvovaginal pruritus			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gingival abscess			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Kidney infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Sinusitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Subcutaneous abscess subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2007	Amendments Requested by Spain Version 'Final 2.0 Amendment 1.1', dated 6 July 2007, incorporated the following changes: • It was clarified that the 2LL visit would only be performed if it was the investigator's opinion that this second look was in the best interest of the subject. • Physical examination and measurement of vital signs added to the baseline visit. • Gynecological examination was included in the physical examination at the screening visit and at the "within 72 hours prior to 2LL visit." • It was clarified that the elective surgery to be undertaken was to be for subjects with known or suspected bilateral ovarian disease. • It was clarified that in the case of a device malfunction, a replacement kit of Adhexil™ could be used. In this situation the total amount of Adhexil™ applied should be approximately 10 mL. • The observation period following initial application of Adhexil™ was extended from 2 minutes to 15 minutes to allow the investigator to assess whether a layer of Adhexil™ had been formed. In addition, it was instructed that during this observation period an air flow was to be maintained to allow the treated surfaces to dry. • The text in the subject information sheet was changed from " Adhexil™ and both laparoscopic procedures will be provided to you free of charge." to read " Adhexil™ and all study specific procedures including the second laparoscopic procedure will be provided to you free of charge."
17 July 2007	Amendments Requested by Germany Version 'Final 2.0 Amendment 2', dated 17 July 2007, incorporated the following changes: • The provision for unopened vials of Adhexil™ to be left at room temperature for up to 24 hours was deleted. • The protocol statement that the investigational product, once aspirated into the application device, was to be used within 4 hours was changed to state that the product was to be used immediately.
02 October 2007	Version 'Final 2.0 IRB Amendment', dated 02 October 2007, incorporated the following changes: • The title of the protocol was changed to "A prospective controlled randomized, multicenter exploratory pilot study evaluating the safety and potential trends in efficacy of Adhexil™ " • An inclusion criterion was added: "Patients with American Society of Anesthesiologists class I (excluding those with a risk of anesthesia complications or those with hypertension)."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 July 2008	PREMATURE TERMINATION OF THE STUDY The study planned to enroll 25 subjects. However, recruitment was much slower than anticipated due to the relatively small number of patients with bilateral ovarian disease and thus a decision was taken to terminate the study after inclusion of 17 subjects.	-

Notes:

Limitations and caveats

None reported