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A Non-interventional Study of postoperative treatment with Goserelin acetate (Zoladex) in moderate to severe endometriosis patients

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NIS REPORT SYNOPSIS

A Non-interventional Study of post-operative treatment with Goserelin acetate (Zoladex) in moderate to severe endometriosis patients

Study Centres:

This study was conducted in 15 centres in China.

Publications:

None at the time of writing this report

Objectives

Primary:

- To evaluate the efficacy of post-operative treatment with Zoladex in moderate to severe endometriosis patients by assessment of proportion of subjects with pelvic symptom recurrence and total recurrence (including pelvic symptom and physical findings) after 18 months since operation.

Secondary:

- To assess the pregnancy rates of infertile subjects receiving post-operative Zoladex treatment after 18 months since operation.
- To observe the administration of Zoladex after operation for the subjects who suffered from severe endometriosis.
- To collect the information of add-back therapy of the subjects who had severe endometriosis and used Zoladex after operation.

Study Design

This was a multi-centre, open-label, non-interventional study to evaluate the efficacy of post-operative treatment with Zoladex in moderate to severe endometriosis patients, which enrolled 408 subjects and was conducted in 15 centres in China.

There were 5 scheduled visits at 0, 3, 6, 12, 18 month in the 18 months observational study since each subject's operation. Zoladex was suggested to be administered every 4 weeks for 3-6 months according to the subject's menstrual cycle.

The subject must sign the Informed Consent Form before any study related activity (e.g., filling out evaluation form) was performed.

Subjects who fulfilled the inclusion/exclusion criteria at visit1 would enter the study with their pelvic symptom score and pregnancy need recorded. Gynaecologic examination, ultrasound examination, pelvic symptom score evaluation and pregnancy status check would be performed every visit since visit 2 (3^{rd} month). Information of add-back treatment was also recorded at every visit. After finishing administration of Zoladex, all subjects were supposed to be observed up to 18 months from operation or confirmed endometriosis relapse or pregnancy. The definition of last visit is either visit 5 (18^{th} month) or the visit with confirmed endometriosis relapse or pregnancy.

Pelvic symptom score was evaluated through Visual Analogue Scale (VAS). The total endometriosis recurrence was confirmed by any confirmatory evidence from VAS, Gynaecologic examination or ultrasound examination.

Target Subject Population and Sample Size

The target subject population were those who had severe endometriosis and were prescribed Zoladex as adjuvant post-operative treatment within one month after operation, which was determined regardless of the subject's recruitment status.

The primary endpoints for this study were the pelvic symptom recurrence rate and the total recurrence rate at the last visit. No tests were conducted and the results primarily presented those rates and their 95% confidence intervals (CI). Assuming the rate is about 15%, to guarantee the width of half 95% CI is less or equal to 3.9% we needed almost 320 evaluable subjects by the formula $1.96 \times \sqrt{\frac{\pi(1-\pi)}{n}} = 3.9\%$. The total enrolled subjects should achieve 400 under the assumption of 20% drop out. If the rate is lower than 15%, the sample size would be even smaller to achieve the same accuracy.

Investigational Product Dosage Form and Strength and Manufacturer

No drug was supplied from AstraZeneca for this non-interventional study. Any drug that needed to be used would be decided and prescribed by investigator.

Zoladex depot 3.6mg, administered subcutaneously every 4weeks for 3-6months, AstraZeneca. (Recommended by the guideline and clinical practice).

Duration of Treatment

Duration of the treatment ranged from 1 to 6 months depending on the number of vials of Zoladex that each subject had been administered, as Zoladex was administered every 4 weeks.

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Criteria for Evaluation

Efficacy

- Primary variables: The pelvic symptom recurrence rate and the total recurrence (including pelvic symptom and physical findings) rate at the last visit (visit 5 or the visit with confirmed endometriosis relapse).

- Secondary variables:

  - Pregnancy rate of four subgroup subjects after operation at visit 5(or last visit)
  - Time from surgery to Zoladex prescription date
  - The proportion of subjects who medicated Zoladex by menstrual cycle
  - Total dose (vials) used in the study and the proportion of subjects in each vials classification
  - The proportion of subjects who had add-back therapy
  - The proportion of subjects who used add-back medicine concomitant with Zoladex
  - The category of add-back medications and the proportion of subjects in each category

Safety

No safety variables were analyzed since this study did not evaluate the safety of Zoladex.

Statistical Method

The primary and secondary variables were summarized for both FAS (Full Analysis Set) and PPS (Per Protocol Set) subjects associated with 2-sided 95% confidence intervals of the rates. No test was performed and efficacy variables were presented with the number and percentage of subjects who had confirmed recurrence.

The administration of Zoladex and the information of add-back therapy were summarized descriptively.

FAS subjects were all subjects who enrolled in this study and took at least one vial of Zoladex. PPS subjects were those in FAS without major protocol violations or deviations.

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Subject Population and Disposition

The subject population and disposition were summarized in Table S1. The study planned to enrol 400 subjects and actually enrolled 408 subjects, among whom396 subjects were included in FAS and 392 subjects in PPS.

Table S1. Subject Population and Disposition (all enrolled subjects)

	Enrolled patients (N=408)
Enrolled patients	408(100.0%)
FAS	396(97.1%)
Patients removed from FAS	12 (2.9%)
PPS	392(96.1%)
Patients removed from PPS	16 (3.9%)

Demographics and Baseline Characteristics

Some demographics and baseline characteristics of FAS subjects were summarized in Table S2. With regard to endometriosis severity score, 203 patients （51.3%） were r-AFS III, and 193 （48.7%）were r-AFS IV, all in the category of severe endometriosis. The mean of baseline VAS score was 4.8 with range from 0 to 10. This fact showed the FAS subjects suffered from obvious pain at the start of study.

Table S2. Demographics and Baseline Characteristics (FAS)

		FAS (N=396)
Demographics		
Age （years）	Mean (S.D)	32.6 (6.27)
	Min ~ Max	19 ~ 53
Pregnancy need (n and % of subjects)	No	235(59.3%)
	Yes	161(40.7%)
Baseline Characteristics		
rAFS score of endometriosis (n and % of subjects)	Ⅲ	203(51.3%)
	Ⅳ	193(48.7%)
Infertility history (n and % of subjects)	No	334(84.3%)
	Yes	62(15.7%)
VAS score	Mean (S.D)	4.8 (3.01)
	Min ~ Max	0 ~ 10

Efficacy Results

Primary Variables

The primary endpoints, the pelvic symptom recurrence rate and the total recurrence rate at the last visit, were presented below for both FAS and PPS subjects in Table S3. After 18 months

study 32 cases were reported with endometriosis recurrence accounting for 8.1% of FAS subjects. Among the 32 recurrence cases, 22 were confirmed by pelvic symptom which accounted for 5.6% of FAS subjects. Little difference was demonstrated between the results of PPS and FAS subjects.

Table S3. Pelvic Symptom Recurrence Rate and Total Recurrence Rate at the Last Visit (FAS/PPS)

	FAS (N=396)		*PPS (N=392)*	
	n(%)	*95%CI*	*n(%)*	*95%CI*
Pelvic symptom recurrence rate (n and % of subjects)	22(5.6%)	3.5% , 8.3%	22(5.6%)	3.6% , 8.4%
Total recurrence rate (n and % of subjects)	32(8.1%)	5.6% , 11.2%	32(8.2%)	5.7% , 11.3%

Secondary Variables

In terms of secondary objectives, the pregnancy rates were summarized considering the classification of infertility histories and pregnancy need in Table S4. Subjects were categorized into 4 subgroups by their answers to the infertility history and pregnancy need in CRF. The highest pregnancy rate of 34.0% was observed in the subgroup consisting of subjects with both infertility history and pregnancy need.

Table S4. Pregnancy Rates at Last Visit (FAS/PPS)

	FAS (N=396)		*PPS (N=392)*	
	n(%)	*95%CI*	*n(%)*	*95%CI*
Pregnancy rate 1 (n and % of subjects)	18(34.0%)	21.5% , 48.3%	18(34.0%)	21.5% , 48.3%
Pregnancy rate 2 (n and % of subjects)	1(11.1%)	0.3% , 48.2%	1(11.1%)	0.3% , 48.2%
Pregnancy rate 3 (n and % of subjects)	24(22.2%)	14.8% , 31.2%	24(22.4%)	14.9% , 31.5%
Pregnancy rate 4 (n and % of subjects)	4(1.8%)	0.5% , 4.5%	4(1.8%)	0.5% , 4.5%

Denominators for each item：
Pregnancy rate 1: Patients with infertility history and with pregnancy need, the denominators of FAS and PPS are both 53；
Pregnancy rate 2: Patients with infertility history and without pregnancy need, the denominators of FAS and PPS are both 9；
Pregnancy rate 3: Patients without infertility history and with pregnancy need, the denominator of FAS is 108 and the denominator of PPS is 107；
Pregnancy rate 4: Patients without infertility history and without pregnancy need, the denominator of FAS is 226 and the denominator of PPS is 223； Every patient in FAS and PPS has pregnant status at the last visit.

The administration of Zoladex included several aspects. The accordance of medication with menstrual cycle and the total vials used were both presented descriptively in Table S5.

Slightly more subjects were administered Zoladex based on their menstrual cycle than those who were not. Most subjects (97.0% of FAS subjects) took no less than 3 vials Zoladex.

Table S5. Administration of Zoladex (FAS/PPS)

		FAS (N=396)	*PPS (N=392)*
Medication by menstrual cycle (n and % of subjects)	No	180(45.5%)	178(45.4%)
	Yes	216(54.5%)	214(54.6%)
Total dose (vials)	Mean (S.D)	4.0 (1.27)	4.0 (1.28)
Total dose (n and % of subjects)	1	4 (1.0%)	4 (1.0%)
	2	8 (2.0%)	8 (2.0%)
	3	189(47.7%)	187(47.7%)
	4	87 (22.0%)	86 (21.9%)
	5	16 (4.0%)	15 (3.8%)
	6	92 (23.2%)	92 (23.5%)

The add-back therapy were summarized in Table S6, including both the number of subjects with add-back therapy and its relation with Zoladex administration. There are 108 subjects (27.3% of FAS subjects) who had add-back therapy and 25 of them (23.1% of subjects with add-back therapy) had their therapy concomitant with Zoladex administration.

Table S6. Summary of Add-back Therapy

		FAS (N=396)	*PPS (N=392)*
Used add-back treatment (n and % of subjects)	No	288(72.7%)	285(72.7%)
	Yes	108(27.3%)	107(27.3%)
Concomitant with Zoladex (n and % of subjects)	No	83 (76.9%)	82 (76.6%)
	Yes	25 (23.1%)	25 (23.4%)
	Total	108(100.0%)	107(100.0%)

Safety

No safety variables were presented because the safety of Zoladex was not evaluated in this study.

Conclusions

- The pelvic symptom recurrence and the total recurrence rates were significantly lower than the recurrence rates of the subjects who only underwent surgery and were not significantly different from the recurrence rates of the subjects who were prescribed Zoladex as post-operative treatment in previous studies. The results demonstrated the similar effectiveness of Zoladex between Chinese and foreign patients.

- The pregnancy rate was far lower than the pregnancy rate of subjects who only underwent surgery. But since no contraception information was collected, it was not feasible to derive any confirmatory conclusion.

- The add-back therapies were mostly used for precaution purposes and no severe side-effect of Zoladex was positively related to the Zoladex administration in the study.

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or special term	Explanation
ANCOVA	Analysis of Covariance
BMI	Body Mass Index
CMH	Cochran-Mantel-Haensel
CRF	Case Report Form
FAS	Full Analysis Set
Max	Maximum
Mean	Mean value
Median	Median value
Min	Minimum
N	Number of samples
Nmiss	Number of cases with missing values
PPS	Per Protocol Set
rAFS	Scoring System of the American Fertility Society（Revised edition）
VAS	Visual Analogue Scale

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1. STUDY SITES

This study was conducted in 15 centres in China including .

All the participating sites and principal investigators with their affiliations, as well as the trial staff at each trial site, are listed in Appendix **B**.

2. PUBLICATIONS

None at the time of writing this report

3. STUDY DATES

First Subject In: 20th Jul 2009
Last Subject Last Visit: 8th Feb 2012

4. BACKGROUND AND RATIONALE

4.1 Background

Endometriosis is the presence of ectopic endometrial tissues outside of the uterus, found most commonly on the pelvic peritoneum or ovary. Endometriosis occurs in 7-10% of women in the general population, including as many as 50% of premenopausal women, 38% (2-50%) of infertile women, and 71-87% of women with chronic pelvic pain. Endometriosis is associated with dysmenorrhea, chronic pelvic pain and infertility. Laparoscopy is the most important diagnostic tool for endometriosis. Extent of the diseases is based on the revised scoring system of the American Fertility Society(R-AFS), established in 1985, with minimal, mild, moderated and severe stages.

Treatment of endometriosis-associated symptom includes both medical and surgical options. Conservative surgery under laparoscopy or laparotomy is frequently the treatment of choice for symptomatic endometriosis, especially in its advanced forms. Currently accepted medical therapies for endometriosis include the weak androgen danazol, gonadotropin-releasing hormone analogues (GnRHa), and oral contraceptives (OC).

The role of surgery, however, has been questioned by the observation that endometriosis is often a progressive disease and that the incidence of relapses is high. The short term recurrence rate of moderate to severe endometriosis is reported to 21.4% at 1 year and 36.5% at 2 year. Recurrence rate is directly related to the stage of the disease, with a 25% recurrence rate in the mild and 61.5% in the severe forms over a 3-year period. The incidence of infertility strictly correlated with endometriosis is difficult to assess, since endometriosis may be coincident with infertility rather than causally related. Nonetheless, it is estimated that between 30% and 50%

of women with endometriosis have some degree of infertility. Several studies reported that GnRHa significantly delays the pelvic symptom recurrence and the recurrence rate. The pregnancy rate among infertile patients receiving post-operatively GnRHa therapy appears to be comparable with those treated with danazol or progestogens. Following 6 months of randomised placebo/GnRHa treatment, the patients treated with GnRHa had significantly fewer clinical symptoms and smaller peritoneal implants at second laparoscopic look. These findings could suggest that medical treatment might delay the recurrence of symptoms associated with endometriosis.

4.2 Rationale for conducting this study

ZOLADEX (goserelin acetate,) is a gonadotrophin-releasing hormone (GnRH) agonist currently marketed for the treatment of endometriosis in China. Although its efficacy and safety have been shown in the previous international multi-centre studies and global registration trial, no data on its real life efficacy in Chinese patients suffered from endometrosis are available. High recurrence rate and low pregnancy rate of post-surgical treatment of moderate/severe endometriosis (EMS) are the key concerns of gynecologists for operation intended to remove visible deposits only. Several publications have approved that medication adjuvant treatment can inhibit estrogen production continuously to eliminate residues and a better efficacy of Zoladex treatment after surgery for moderate to severe endometriosis in terms of pain-free interval and recurrence rate. Given the difficulty to measure disease relapse by invasive examination in routine practice, we select the symptom rating scale as a relevant symptom presence.

5. OBJECTIVES

5.1 Primary objectives

- To evaluate the efficacy of post-operative treatment with Zoladex in moderate to severe endometriosis patients by assessment of proportion of subjects with pelvic symptom recurrence and total recurrence (including pelvic symptom and physical findings) after 18 months since operation.

5.2 Secondary objectives

- To assess the pregnancy rates of infertile subjects receiving post-operative Zoladex treatment after 18 months since operation.
- To observe the administration of Zoladex after operation for the subjects who suffered from severe endometriosis.
- To collect the information of add-back therapy of the subjects who had severe endometriosis and used Zoladex after operation.

6. STUDY DESIGN AND SELECTION CRITERIA

6.1 Overall study design and flow chart

This was an open, observational, multi-centre study performed in 15 centres. 400 patients were planned to be recruited with approximately 27 patients per centre.

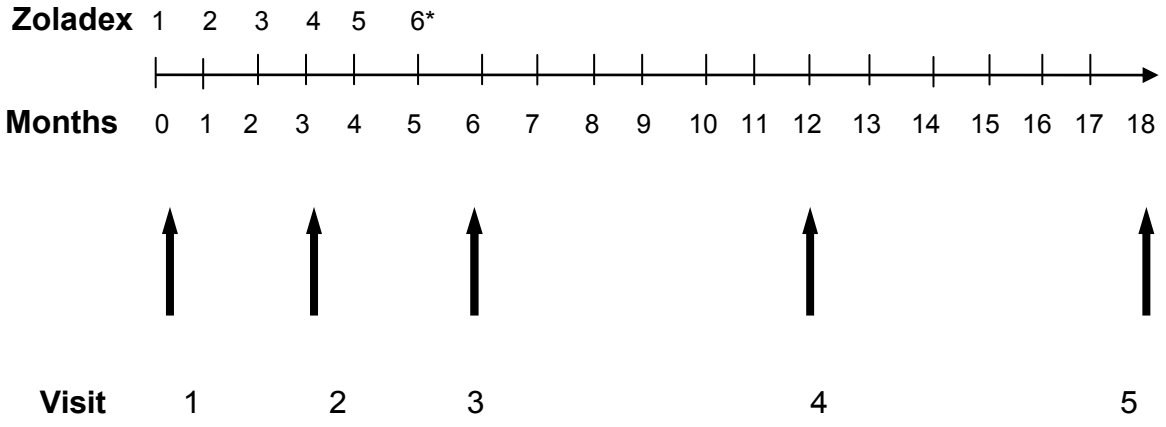
The patient must sign the Informed Consent Form before any study related activity (e.g., filling out evaluation form) would be performed.

Before the patient recruitment, the investigator had decided to prescribe Zoladex as adjuvant treatment to the patient, which was independent from the patient recruitment. Patient who fulfilled all inclusion/exclusion criteria at visit 1 could enter this study, and the patients' symptom score and pregnancy need would also be recorded at visit 1, visit 2 (3 months post operation), visit 3 (6 months post operation), visit 4 (12 months post operation) and visit 5 (18 months post operation). The definition of last visit was either visit 5 or the time with confirmed disease relapse or pregnancy. Based on local clinical practice, approximately 60-80% of patients were to be treated with GnRHa for 3 months. (Please refer to the relative paragraph in local or national guidelines on endometriosis diagnosis and treatment).

During Visit 1~5, symptom score would be collected according to physician's judgement and recorded in Out-patient medical records.

For the time of administration of Zoladex and scheduled visits, please see Figure 1.

Figure 1 Study flow chart



**Note: Goserelin acetate (Zoladex) depot 3.6mg, administered subcutaneously every 4weeks for 3-6months (Recommended by the guideline and clinical practice).*

For the list of examination terms that were conducted at each visit, please see Table 1.

Table 1. Study Plan

Visit	**1**	**2**	**3**	**4**	**5**
Month(±No. Week)	0M	3M (±1w)	6M (±1w)	12M (±1w)	18M (±1w)
Written Inform Consent Form	X				
Medical History	X				
Inclusion/exclusion Criteria	X				
Physical Examination	X				
Gynaecologic examination		X	X	X	X
Ultrasound[1]		X	X	X	X
VAS score[2]	X[3]	X	X	X	X
Pregnancy[4]	X	X	X	X	X
Investigator Assessment Report[5]					X
Add-back treatment[1]	X	X	X	X	X

1 Based on normal clinical practice
2 A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. Operationally a VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in millimetres from the left hand end of the line to the point that the patient marks.
3 Pre-operative symptom score.
4 The pregnancy need and ART plan will be recorded at visit 1. The pregnancy will be recorded during the continuous visits.
5 Assessment content including: Good (No recurrence, Good feedback from patients); Neutral (No recurrence, Neutral feedback from patients); Poor(Recurrence).

6.2 Selection of patient population

Patient population should be selected without bias.

Investigator(s) must keep a record of patients who entered pre-trial screening but were never enrolled. Each patient must meet all of the inclusion criteria and none of the exclusion criteria for this study. Under no circumstances could there be exceptions to this rule.

6.2.1 Inclusion criteria

For inclusion in the study patients must fulfil the following criteria.

1. Advanced endometriosis confirmed histologically (r-AFS score III-IV) with conservative laparoscopy or laparotomy.

2. Patient who had the indication of Zoladex and had been prescribed Zoladex according to physician's judgement, irrespective of the inclusion in the study.

3. Patient had been prescribed Zoladex within 1 month after operation.

4. Provision of written informed consent prior to any study specific procedures

6.2.2 Exclusion criteria

Patients must not enter the study if any of the following exclusion criteria are fulfilled

1. Have used hormone treatment within 3 months before recruitment.

2. Involvement in the planning and conduct of the study (applies to both AstraZeneca staff or staff at the study site)

3. Previous enrolment in the present study

6.2.3 Discontinuation of subjects from study

6.2.3.1 Criteria for discontinuation

Patients may be discontinued from study treatment and assessments at any time. Specific reasons for discontinuing a patient are:

- Voluntary discontinuation by the patient who is at any time free to discontinue his/her participation in the study, without prejudice to further treatment
- Risk to patients as judged by the investigator and /or AstraZeneca
- Incorrectly enrolled patients
- Patient lost to follow-up
- Adverse Events（judged by an investigator）

6.2.3.2 Procedures for discontinuation

Subjects were free to discontinue their participation in the study at any time, without prejudice to their treatment. Subjects who discontinued should always be asked about the reason(s) for their discontinuation and if possible, subjects should be seen and assessed by an investigator(s).

7. TARGET PATIENT POPULATION, STUDY DISEASE (IF APPLICABLE) AND SAMPLE SIZE

7.1 Target patient population

The target subject population were those who had severe endometriosis and were prescribed Zoladex as adjuvant post-operative treatment within one month after operation, which was determined regardless of the subject's recruitment status.

7.2 Study disease

Advanced endometriosis confirmed histologically (r-AFS score III-IV) with conservative laparoscopy or laparotomy

7.3 Sample size

The primary endpoints for this study were the pelvic symptom recurrence rate and the total recurrence rate at the last visit. No tests were conducted and the results primarily presented those rates and their 95% confidence intervals (CI). Assuming the rate is about 15%, to guarantee the width of half 95% CI is less or equal to 3.9% we needed almost 320 evaluable subjects by the formula $1.96 \times \sqrt{\frac{\pi(1-\pi)}{n}} = 3.9\%$. The total enrolled subjects should achieve 400 under the assumption of 20% drop out. When the rate is lower than 15%, the required sample size would be even smaller to achieve the same accuracy.

8. CRITERIA FOR EVALUATION (MAIN VARIABLES)

8.1 Summary of efficacy variables and their study objectives

Table 2 summarizes the efficacy variables and shows how they related to the study objectives.

Table 2. Summary of efficacy variables and their study objectives

Objectives	Outcome variables
Primary	
To evaluate the efficacy of post-operative treatment with Zoladex in moderate to severe endometriosis patients.	The pelvic symptom recurrence rate and the total recurrence (including pelvic symptom and physical findings) rate at the last visit (visit 5 or the visit with confirmed endometriosis relapse)
Secondary	
To assess the pregnancy rates of infertile subjects receiving post-operative Zoladex treatment after 18 months since operation.	Pregnancy rate of four subgroup subjects after operation at visit 5(or last visit)

To observe the administration of Zoladex after operation for the subjects who suffered from severe endometriosis.	Time from surgery to Zoladex prescription date
	The proportion of subjects who medicated Zoladex by menstrual cycle Total dose (vials) used in the study and the proportion of subjects in each vials classification
To collect the information of add-back therapy of the subjects who had severe endometriosis and used Zoladex after operation.	The proportion of subjects who had add-back therapy
	The proportion of subjects who used add-back medicine concomitant with Zoladex The category of add-back medications and the proportion of subjects in each category

8.2 Primary variables

The pelvic symptom recurrence rate and the total recurrence (including pelvic symptom and physical findings) rate at the last visit (visit 5 or the visit with confirmed endometriosis relapse).

The total recurrence in this study is defined as the occurrence of one or more of the followings:

- Recurrence of pelvic pain: with pelvic pain severity equal to or greater than before surgery self-reported by the woman;
- Twice ultrasound (interval time≥4 weeks) diagnosis of endometriosis, and the cyst diameter is no less than 3cm after ultrasound examination;
- Clinical findings suggesting a recurrence (pelvic masses, pelvic tenderness, or nodulations at pelvic examination)

8.3 Secondary variables

- Pregnancy rate of four subgroup subjects after operation at visit 5(or last visit)
- Time from surgery to Zoladex prescription date

- The proportion of subjects who medicated Zoladex by menstrual cycle
- Total dose (vials) used in the study and the proportion of subjects in each vials classification
- The proportion of subjects who had add-back therapy
- The proportion of subjects who used add-back medicine concomitant with Zoladex
- The category of add-back medications and the proportion of subjects in each category

8.4 Safety variables

No safety variables were presented because the safety of Zoladex was not evaluated in this study.

9. STATISTICAL METHODS

In general, Descriptive statistics were used for the summary of variables. Continuous variables were presented using n, mean, standard deviation, medium, minimum and maximum, and categorical variables were summarized using n and percentage. Where appropriate, all the summaries of variables will be presented by visit and graphics might be used to facilitate the presentation.

All the efficacy variables were presented using descriptive statistics. The co-primary endpoints of pelvic symptoms recurrence rate and total recurrence rate were presented using proportion and its 95% confidence interval. Pregnancy rates will be presented in the similar way as for the primary endpoint. The add-back therapy was described by classifying and listing all the add-back medications.

Baseline values were those measurements taken at visit 1.

9.1 Population Analysis Sets:

9.1.1 Definition of the target population

Full Analysis Set (FAS)

The FAS included all patients who met inclusion/exclusion criteria and took at least one dose of study drug. All the analyses for this study were based on FAS.

Per Protocol Set (PPS)

The PPS was a subset of FAS excluding patients with major protocol violations. PPS was mainly used from primary and secondary efficacy analyses.

Major Protocol Deviations

The case when data of some visits were completely missing.

9.2 Statistical Analysis Result

9.2.1 Study subject dispositions

A total of 408 patients were enrolled in this study, including 311 (76.2%) who completed visit 5 (the last scheduled visit) without recurrent endometriosis or pregnancy, and 31 (7.6%) who discontinued due to recurrent endometriosis. Compliance with one or more of the diagnostic evidences for recurrent endometriosis, including gynecologic examination, B-ultrasound or VAS score, would constitute a confirmed recurrent endometriosis. See the "diagnostic evidence for recurrent endometriosis" column for the specific diagnostic evidences for confirmed recurrence in the 31 patients.

47 patients (11.5%) discontinued due to pregnancy, including one patient who was pregnant with VAS-confirmed recurrence at the last visit and discontinued for the pregnancy. There was therefore 1 more patient included in pain recurrence group than in VAS score-confirmed recurrence group, and thus the number of patients who had endometriosis recurrence was 32 instead of 31.

Two patients, Patients No. 1001 and 1032, were discontinued due as "enrollment error": Patient 1032 discontinued on the day of enrollment, i.e., 20 December 2009, and Patient 1001 was enrolled on 7 December 2009 and discontinued on 28 February 2010. There were fewer patients discontinued due to enrollment error than the patients who had violation of inclusion/exclusion criteria because some patients continued the study and discontinued for other reasons despite inclusion/exclusion violations. See Table 3 for details.

Besides the 408 patients enrolled , other 18 patients also attended the study but were excluded. Among the 18 patients, 2 had their first visit done before their signature of ICF, and the other 16 patients were excluded since they signed the ICF before its approval by the ethic committee of the hospital.

Table 3. Summary of patients' enrollment and completion status (all enrolled patients)

	Enrolled patients (N=408)
Enrolled patients	408(100.0%)
Discontinuations（all enrolled patients）	408(100.0%)
Completed V5 without relapse or pregnancy	311(76.2%)
Recurrent endometriosis	31 (7.6%)
Diagnostic evidence for recurrent endometriosis：	-
Gynecologic exam only	3 (9.7%)
B-ultrasound only	4 (12.9%)
VAS only	16 (51.6%)
Gynecologic exam and B-ultrasound	3 (9.7%)
B-ultrasound and VAS	2 (6.5%)

Gynecologic exam, B-ultrasound and VAS	3 (9.7%)
Pregnancy	47 (11.5%)
Patient voluntary discontinuations	1 (0.2%)
Loss to follow-up	15 (3.7%)
Further participation inappropriate at investigator's discretion	1 (0.2%)
Enrollment error	2 (0.5%)

Notes: When calculating the number and percentage of diagnostic evidence for recurrent endometriosis, the number of patients with recurrent endometriosis is used as the denominator; while other percentages are calculated with the number of enrolled patients being the denominator.
There were 32 patients who had endometriosis recurrence at the 5th visit or the last visit. One of them was categorized as 'Pregnancy' since she was pregnant at the same time.

396 patients (97.1%) were included in FAS and 12 were excluded from FAS, including 4 (0.9%) for violation of inclusion/exclusion criteria: one patient failed inclusion criterion 1, as the endometriosis was not r-AFS score III-IV, and three patients failed inclusion criterion 2, as Zoladex was prescribed later than the time of enrollment. Aside from the 4 patients, there were additional patients who had violation of inclusion/ exclusion criteria but were removed from any statistical analysis set due to other more serious protocol violations. 8 patients (1.9%) were considered as having not used study drug because their data were missing since the first visit following drug dispensing and therefore their Zoladex administration status was unknown. Four patients (1.0%) had missing visits: Patients 1409 and 1427 were missing for visit 4, and Patients 1907 and 1910 were missing for visit 3. See Table 4 for the specific reasons for removals from any statistical analysis set.

Table 4. Summary of statistical analysis sets (all enrolled patients)

	Enrolled patients (N=408)
Enrolled patients	408(100.0%)
FAS	396(97.1%)
Patients removed from FAS	12 (2.9%)
Violated incl. criterion 1：Advanced endometriosis confirmed histologically (r-AFS score III-IV) with conservative laparoscopy or laparotomy	1 (0.2%)
Violated incl. criterion 2：Patient who has the indication of Zoladex and has been prescribed Zoladex according to physician's judgement, irrespective of the inclusion in the study	3 (0.7%)
Study drug use unknown	8 (2.0%)
PPS	392(96.1%)
Patients removed from PPS	16 (3.9%)
Missing visits	4 (1.0%)
Violated incl. criterion 1：Advanced endometriosis confirmed histologically (r-AFS score III-IV) with conservative laparoscopy or laparotomy	1 (0.2%)
Violated incl. criterion 2：Patient who has the indication of Zoladex and has been prescribed Zoladex according to physician's judgement, irrespective of the inclusion in the study	3 (0.7%)
Study drug use unknown	8 (2.0%)

Notes: Denominator of percentage is the number of patients in the analysis set. Patients who missed data of all the visits after drug distribution were categorized into Study drug use unknown.

9.2.2 Demographics and baseline characteristics

All the 396 patients in the FAS had their baseline age, weight, height, BMI and heart rate observed. Among them, 161 (40.7%) had pregnancy need, including 53 (32.9%) with infertility history. 5 patients (1.3%) in the FAS had assisted reproductive technology planned. See Table 5 for details.

Table 5. Demographics and other baseline characteristics (FAS)

Parameter		*FAS (N=396)*
Age （years）	N(Nmiss)	396(0)
	Mean(S.D)	32.6(6.27)
	Median	32.0
	Min~Max	19~53
Weight（kg）	N(Nmiss)	396(0)
	Mean(S.D)	55.9(8.14)
	Median	55.0
	Min~Max	39~93
Height（cm）	N(Nmiss)	396(0)
	Mean(S.D)	161.7(4.53)
	Median	162.0
	Min~Max	149~175
BMI（kg/m^2）	N(Nmiss)	396(0)
	Mean(S.D)	21.36(2.973)
	Median	20.80
	Min~Max	14.7~36.5
Heart rate （beats/min）	N(Nmiss)	396(0)
	Mean(S.D)	77.2(7.69)
	Median	78.0
	Min~Max	60~115
Pregnancy need	No	235(59.3%)
	Yes	161(40.7%)
	Total	396(100.0%)
Assisted reproductive technology planned	No	391(98.7%)
	Yes	5(1.3%)
	Total	396(100.0%)

Notes: Percentages are calculated with number of non-missing cases being the denominator. The total is the number of non-missing cases, and number of missing cases is the difference between the number of FAS patients and the total.
N (Nmiss): N indicates non-missing cases of the respective parameter, and Nmiss indicates missing cases: the sum of both is the number of the patients in analysis set. S.D: standard deviation.

9.2.3 Medical and surgical history

Among the 396 patients in the FAS, 62 (15.7%) had infertility history. The mean time from surgery to informed consent was 17.14 days (S.D 17.79 days), median 8 days, and range 1 to 87 days. All the 396 patients had at least one surgery. Among those who underwent cystectomy or adnexectomy, 351 (88.6%) underwent cystectomy only, 8 (2.0%) underwent adnexectomy only, and 7 (1.8%) underwent both; a total of 130 patients (32.8%) received surgeries other than these two. Please note that one patient might have received more than one surgical treatment. That was why the sum of all the numbers of subjects in the four classes exceeded 396. With regard to endometriosis severity score, 203 patients (51.3%) were r-AFS III and 193 (48.7%) were r-AFS IV. See Table 6 for details.

Table 6. Summary of medical history, informed consent status and surgical history (FAS)

Parameter		*FAS (N=396)*
Infertility history	No	334(84.3%)
	Yes	62(15.7%)
	Total	396(100.0%)
Time from surgery to informed consent (days)	N(Nmiss)	396(0)
	Mean(S.D)	17.14(17.79)
	Median	8.00
	Min~Max	1.0~87.0
Surgery type	At least one surgery	396(100.0%)
	Cystectomy	351(88.6%)
	Adnexectomy	8(2.0%)
	Cystectomy & Adnexectomy	7(1.8%)
	Other	130(32.8%)
rAFS score of endometriosis	Ⅲ	203(51.3%)
	Ⅳ	193(48.7%)
	Total	396(100.0%)

Notes: Percentages are calculated with number of non-missing cases being the denominator. The total is the number of non-missing cases, and number of missing cases is the difference between the number of FAS patients and the total.

N (Nmiss): N indicates non-missing cases of the respective parameter, and Nmiss indicates missing cases: the sum of both is the number of the patients in analysis set. SD: standard deviation.

For "surgery type", the percentages are calculated using the number of patients with at least one surgery as the denominator.

9.2.4 Primary objective

In the FAS population of this study, at the last visit, 22 cases (5.6%) from total 396 patients had pelvic symptom recurrence, with 95% CI of pelvic symptom recurrence rate ranging from 3.5% to 8.3%. These were patients whose endometriosis recurrence was confirmed by VAS score. The number of disease-recurrent patients was 32 (8.1%) and 95% CI of endometriosis

recurrence rate was (5.6%, 11.2%). The results for the PPS population were similar. See Table 7 for details.

Table 7. Pelvic symptom recurrence rate and endometriosis recurrence rate at the last visit (FAS/PPS)

	Data set			
	FAS (N=396)		*PPS(N=392)*	
Parameter	*n(%)*	*95 %CI*	*n(%)*	*95 %CI*
Recurrence rate of pelvic pain symptom	22(5.6%)	3.5% , 8.3%	22(5.6%)	3.6% , 8.4%
Total recurrence rate	32(8.1%)	5.6% , 11.2%	32(8.2%)	5.7% , 11.3%

Notes: Percentages are calculated with number of non-missing cases being the denominator. All the 396 patients in FAS and 392 patients in PPS have their pelvic symptom recurrence and endometriosis recurrence evaluated.

Descriptive statistics were presented for VAS scores and their changes from baseline at each visit for all patients in FAS and PPS. The mean baseline VAS score in the 396 patients was 4.8 (S.D 3.01), median 5 and range 0 to 10; mean VAS score at visit 2 was 0.7 (S.D 1.38), median 0 and range 0 to 7; and mean VAS score at the last visit was 0.9 (S.D 1.70), median 0 and range 0 to 10. A median of 0 indicated that more than half of the patients had the VAS score 0. See Table 8 for the detailed VAS scores and their changes from baseline for each visit. With the number of discontinued patients increasing along visits, the number of patients with missing VAS scores also increased as the study continued. The “last visit” refers to visit 5 or the last visit at which the patient discontinued and therefore there were no missing VAS scores in the last visit.

The pelvic pain reflected by the VAS score was significantly reduced at visit 2 which is the visit after the administration of the first 3 vials Zoladex. After visit 2, the pelvic pain for the majority of all patients stayed steady at a very low level up to the end of the follow-up period.

Table 8. Summary of VAS scores by visit (FAS/PPS)

		Data Set			
		FAS (N=396)		*PPS (N=392)*	
Visit		*Value*	*Change from baseline*	*Value*	*Change from baseline*
Baseline	N(Nmiss)	396(0)		392(0)	
	Mean(S.D)	4.8(3.01)		4.7(3.02)	
	Median	5.0		5.0	
	Min,Max	0, 10		0, 10	
Visit 2	N(Nmiss)	395(1)	395(1)	391(1)	391(1)
	Mean(S.D)	0.7(1.38)	-4.1(2.94)	0.7(1.39)	-4.0(2.95)
	Median	0.0	-4.0	0.0	-4.0
	Min,Max	0, 7	-10, 1	0, 7	-10, 1

Visit 3	N(Nmiss)	387(9)	387(9)	385(7)	385(7)
	Mean(S.D)	0.7(1.39)	-4.0(2.85)	0.7(1.40)	-4.0(2.85)
	Median	0.0	-4.0	0.0	-4.0
	Min,Max	0, 8	-10, 2	0, 8	-10, 2
Visit 4	N(Nmiss)	361(35)	361(35)	359(33)	359(33)
	Mean(S.D)	0.8(1.60)	-3.9(2.88)	0.8(1.60)	-3.9(2.87)
	Median	0.0	-4.0	0.0	-4.0
	Min,Max	0, 10	-10, 4	0, 10	-10, 4
Visit 5	N(Nmiss)	330(66)	330(66)	326(66)	326(66)
	Mean(S.D)	0.8(1.47)	-4.0(2.86)	0.8(1.47)	-3.9(2.86)
	Median	0.0	-4.0	0.0	-4.0
	Min,Max	0, 10	-10, 6	0, 10	-10, 6
Last visit	N(Nmiss)	396(0)	396(0)	392(0)	392(0)
	Mean(S.D)	0.9(1.70)	-3.9(2.97)	0.9(1.71)	-3.9(2.97)
	Median	0.0	-4.0	0.0	-4.0
	Min,Max	0, 10	-10, 6	0, 10	-10, 6

Notes: N (Nmiss): N indicates non-missing cases of the respective parameter, and Nmiss indicates missing cases: the sum of both is the number of the patients in analysis set. S.D: standard deviation.
Last visit was the 5th visit for patients who ended the study as scheduled. For those who ended the study before or after the 5th visit, last visit referred to the last time of visit when the data was available.

9.2.5 Secondary objectives

9.2.5.1 Pregnancy rate

A total of 47 patients in the FAS were pregnant at the last visit. Among the 53 patients with infertility history and pregnancy need, 18 were pregnant, contributing to a pregnancy rate of 34.0%, with 95% CI (21.5%, 48.3%). Among the 9 patients in both FAS and PPS with infertility history but without pregnancy need, 1 was pregnant, contributing to a pregnancy rate of 11.1%, 95% CI (0.3%, 48.2%). Among the 108 patients in the FAS without infertility history and with pregnancy need, 24 were pregnant, contributing to a pregnancy rate of 22.2%, 95% CI (14.8%, 31.2%). Among the 226 patients in the FAS without infertility history and without pregnancy need, 4 were pregnant, contributing to a pregnancy rate of 1.8%, 95% CI (0.5%, 4.5%). See Table 9 for details.

Table 9. Summary of pregnancy rates at the last visit (FAS/PPS)

	Data set			
	FAS (N=396)		*PPS (N=392)*	
Parameter	*n(%)*	*95 %CI*	*n(%)*	*95 %CI*
Pregnant rate 1	18(34.0%)	21.5% , 48.3%	18(34.0%)	21.5% , 48.3%
Pregnant rate 2	1(11.1%)	0.3% , 48.2%	1(11.1%)	0.3% , 48.2%
Pregnant rate 3	24(22.2%)	14.8% , 31.2%	24(22.4%)	14.9% , 31.5%
Pregnant rate 4	4(1.8%)	0.5% , 4.5%	4(1.8%)	0.5% , 4.5%

Notes: Denominators for each item：Pregnant rate 1. Patients with infertility history and with pregnancy need, the denominators of FAS and PPS are both 53；Pregnant rate 2. Patients with infertility history and without pregnancy need, the denominators of FAS and PPS are both 9；Pregnant rate 3. Patients without infertility history and with pregnancy need, the denominator of FAS is 108 and the denominator of PPS is 107；Pregnant rate 4. Patients without infertility history and without pregnancy need, the denominator of FAS is 226 and the denominator of PPS is 223；Every patient in FAS and PPS has pregnant status at the last visit.

9.2.5.2 Medicine administration

Among the 396 patients in FAS, the mean time from surgery to prescription was 7.6 days (S.D 8.43), median 4.0 days and range -9 to 31 days, with only one patient (No. 0319) having prescription date (Nov 15th 2009) earlier than the surgery date (Nov 14th 2009). After prescription, the patient underwent surgery in another hospital, so that the prescription date was not the actual medication date, which was later than the surgery date.

216 patients (54.5%) received medication by menstrual cycle. The mean of total dose was 4 vials, with median 3 vials and range 1 to 6 vials. Among them, 4 (1.0%) used 1 vial; 8 (2.0%) used 2 vials; 189 (47.7%) used 3 vials; 87 (22.0%) used 4 vials; 16 (4.0%) used 5 vials and 92 (23.2%) used 6 vials. See Table 10 for details.

Table 10. Summary of prescription and medication status (FAS/PPS)

Parameter		*Data set*	
		FAS (N=396)	*PPS (N=392)*
Time from surgery date to prescription date (days)	N(Nmiss)	396(0)	392(0)
	Mean(S.D)	7.6(8.43)	7.6(8.46)
	Median	4.0	4.0
	Min,Max	-9, 31	-9, 31
Medication by menstrual cycle	No	180(45.5%)	178(45.4%)
	Yes	216(54.5%)	214(54.6%)
	Total	396(100.0%)	392(100.0%)
Total dose (vials)	N(Nmiss)	396(0)	392(0)
	Mean(S.D)	4.0(1.27)	4.0(1.28)
	Median	3.0	3.0
	Min,Max	1, 6	1, 6
Total dose	1	4 (1.0%)	4 (1.0%)
	2	8 (2.0%)	8 (2.0%)
	3	189(47.7%)	187(47.7%)
	4	87 (22.0%)	86 (21.9%)
	5	16 (4.0%)	15 (3.8%)
	6	92 (23.2%)	92 (23.5%)
	Total	396(100.0%)	392(100.0%)

Notes: Percentages are calculated with number of non-missing cases being the denominator. The total is the number of non-missing cases, and number of missing cases is the difference between the number of patients in analysis set and the total.

N (Nmiss): N indicates non-missing cases of the respective parameter, and Nmiss indicates missing cases: the sum of both is the number of the patients in analysis set. S.D: standard deviation.

9.2.5.3 Add-back therapy

108 of the 396 patients in the FAS (27.3%) received add-back treatments, including 25 (23.1%) who received treatments concomitant with Zoladex and 83 (76.9%) not concomitant with Zoladex. See Table 11 for details of add-back treatments of both FAS and PPS patients.

Among the 108 patients with add-back treatment, 18 (4.5%), used estrogens, 4 (1.0%) used progestogens, 1 (0.3%) used estrogen and progestogen combinations, 74 (18.7%) used other estrogens, 1 (0.3%) used pregnene derivatives, 6 (1.5%) used other gynecologicals, and 27 (6.8%) used calcium carbonate+vitamin. See Table 12 for details.

Table 11. Summary of add-back treatments (FAS/PPS)

Parameter		*Data set*	
		FAS (N=396)	*PPS (N=392)*
Used add-back treatment	No	288(72.7%)	285(72.7%)
	Yes	108(27.3%)	107(27.3%)
	Total	396(100.0%)	392(100.0%)
Concomitant with Zoladex	No	83 (76.9%)	82 (76.6%)
	Yes	25 (23.1%)	25 (23.4%)
	Total	108(100.0%)	107(100.0%)

Notes: For "Used add-back treatment"， percentages are calculated with number of non-missing cases being the denominator. For "Concomitant with Zoladex", percentages are calculated with number of cases using add-back treatment being the denominator.

Table 12. Summary of add-back medications as categorized (FAS/PPS)

	Data set	
	FAS (N=396) *n (%)*	*PPS (N=392)* *n (%)*
At least one add-back medication	108(27.3%)	107(27.3%)
Other estrogens	74 (18.7%)	73 (18.6%)
LIVIAL	74 (18.7%)	73 (18.6%)
Vitamins with minerals	27 (6.8%)	27 (6.9%)
CALCIUM CARBONATE+VITAMIN D NOS	27 (6.8%)	27 (6.9%)
Estrogens	18 (4.5%)	18 (4.6%)
ESTRADIOL VALERATE	10 (2.5%)	10 (2.6%)
PREMARIN (ESTROGENS CONJUGATED)	7 (1.8%)	7 (1.8%)
ESTROGENS CONJUGATED	1 (0.3%)	1 (0.3%)
OTHER GYNECOLOGICALS	6 (1.5%)	6 (1.5%)
REMIFEMIN	6 (1.5%)	6 (1.5%)
Progestogens	4 (1.0%)	4 (1.0%)
MEDROXYPROGESTERONE	4 (1.0%)	4 (1.0%)
Pregnen (4) derivatives	1 (0.3%)	1 (0.3%)

PROGESTERONE	1 (0.3%)	1 (0.3%)
Progestogens and estrogens, fixed combinations	1 (0.3%)	1 (0.3%)
DROSPIRENONE+ETHINYLESTRADIOL	1 (0.3%)	1 (0.3%)

Notes: Percentage using number of cases with add-back treatment in each data set as the denominator.

10. SAFETY

The safety of Zoladex and add-back medicine is not evaluated in the study.

11. ETHICS

11.1 Ethics and regulatory review

An Ethics Committee approved the final study protocol, including the final version of the Informed Consent Form and any other written information to be provided to the patients. The investigator ensured the distribution of these documents to the applicable Ethics Committee, and to the study site staff.

The opinion of the Ethics Committee was given in writing. The investigator submitted the written approval to AstraZeneca before enrolment of any patient into the study.

AstraZeneca approved the modifications to the Informed Consent Form that were needed to meet local requirements.

11.2 Ethical conduct of the study

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy.

11.3 Informed consent

The principal investigator(s) at each centre had:

- Ensured that the patient was given full and adequate oral and written information about the nature and purpose of the study.
- Ensured that the patients were notified that they are free to discontinue from the study at any time.
- Ensured that the patient were given the opportunity to ask questions and allowed time to consider the information provided.

- Obtained and documented the patient's signed and dated informed consent before conducting any procedure specifically for the study.
- Ensured the original, signed Informed Consent Form was stored in the Investigator's Study File.
- Ensured a copy of the signed Informed Consent Form was given to the patient.

11.4 Patient data protection

The Informed Consent Form had incorporated (or, in some cases, be accompanied by a separate document incorporating) wording that complied with relevant data protection and privacy legislation.

11.5 Audits and inspections

Authorized representatives of AstraZeneca, a regulatory authority, or an Ethics Committee had performed audits or inspections at the centre, including source data verification. The purpose of an audit or inspection was to systematically and independently examine all study-related activities and documents, to determine whether these activities were conducted, and data were recorded, analysed, and accurately reported according to the protocol, Good Clinical Practice (GCP), guidelines of the International Conference on Harmonisation (ICH), and any applicable regulatory requirements. The investigator should contact AstraZeneca immediately when contacted by a regulatory agency about an inspection at the centre.

12. DISCUSSION

As some historical researches showed, the pelvic symptom recurrence rate of patients, who only took cystectomy, at the 2nd year after operation was about 10% and 15.8% in the randomized controlled trial (RCT) reported by Beretta in 1998 and in the RCT reported by Alborzi in 2004 respectively [13]. Another clinical study which included 269 women undergoing conservative surgery for mild or severe endometriosis showed the pelvic symptom recurrence rate at one- and two-year follow up visits were 13.1% and 23.5% for the Goserelin group comparing with 21.4% and 36.5% for the expectant group [5]. A study conducted among 225 Chinese patients who took laparoscope surgery for severe endometriosis at two hospitals between 1999 and 2003 demonstrated that the endometriosis recurrence rate after two years from the laparoscope surgery was about 10.3% for the Goserelin group comparing with 23.4% for the Gestrinone group, 24.1% for the Danazol group and 42.2% for the non post-surgical medication group [14].

The result of this study showed similar endometriosis recurrence rate to the previous researches, where patients received surgery and Goserelin as post-surgical treatment, with the total recurrence rate being 8.1% and its 95% CI ranging from 5.6% to 11.2%. Consequently, it showed no significant difference on the efficacy of Zoladex between Chinese patients and foreign patients. Both pelvic symptom recurrence rate and endometriosis recurrence rate were obviously different from those of patients only undergoing surgery in several historical studies.

The pelvic symptom recurrence rate was 5.6% and its 95% CI was (3.5%, 8.3%), which could be stated as significantly less than the pelvic symptom recurrence rate 10% and 15% in two RCT reported by Beretta in 1998 and by Alborzi in 2004 respectively [13]. The total recurrence rate was also significantly less than 42.2%, which is the endometriosis recurrence rate in a study conducted on Chinese patients between 1999 and 2003 [14].

The VAS score of the study population at visit 2 decreased significantly from baseline which lowered down by85%, from 4.8 to 0.7. The mean of VAS score stayed slightly above 0 and the median was 0 for all the following visits up to the end of the study. It indicated that more than half of the patients were getting rid of the pelvic pain after visit 2 and Zoladex had great effect on pelvic pain symptom control as the pain caused by endometriosis would not subside spontaneously.

The pregnancy rate of the patients who only underwent surgery was about 50% in some historical studies [13]. A similar result was presented in a study of 276 patients with endometriosis treated by laparoscope operation. The pregnancy rate of the group with Goserelin as post-operative treatment was 57.5% [15].

The overall pregnancy rate of this study was 11.9% and significantly less than 50%. Since the data gave no clue about how many patients used chemical or mechanical contraception after operation, it was not feasible to derive any conclusion about the influence of Zoladex on conception.

The influence of administration Zoladex on study patients' conception was not confirmatory. Although all pregnancy rates of the four subgroups studied were obviously lower than 50% and the overall pregnancy rate was 11.9%, it was far from being conclusive since only 161 (40.7%) patients had pregnancy need and the contraception information was not collected for all patients. Another study on Chinese population from 1999 to 2004 showed that administration of Zoladex as post-operative treatment did not reduce pregnancy rate which made us to ponder before drawing a conclusion directly based on the data of this study [15].

Among the 396 patients in FAS, 108 (27.3%) used add-back medicine which was not a big portion. Among these 108 patients with add-back therapy, only 25 (23.1%) patients administered add-back medicine concomitant with Zoladex which showed most patients used add-back medicine for precaution purposes and not because of the severe side-effect of Zoladex. Since no bone mineral density was estimated, it could be concluded from the existing data that Zoladex had little side-effect which needed add-back therapy.

13. DATE OF THE REPORT

31 Jul 2012

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