



Judicial medical management of mild and minimal endometriosis in selected patients of infertility is non-inferior to surgical treatment – a retrospective analysis

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Abstract

Background: Endometriosis is an enigmatic disease that affects approximately 10% of women of reproductive age and almost 50% of women with endometriosis experience infertility. These women experience symptoms of dysmenorrhea, premenstrual pain, dyspareunia, and infertility, but many affected women are asymptomatic.

Objective: To analyse the clinical pregnancy rate after treating mild and minimal endometriosis causing infertility with dienogest (2 mg) or by surgical intervention.

Materials and Methods: 146 subfertile women with mild and minimal endometriosis, enrolled over a period of 36 months (January 2017 to December 2019) at Calcutta Fertility Mission have been included in the present study. They were grouped in A and B and treated with dienogest (2mg) for 90days or by laparoscopic ablation, and ovulation induction. Clinical pregnancy rates were analysed.

Results: In our study, 18.52% of patients with early stage asymptomatic endometriosis, had conceived spontaneously after treatment with dienogest for 3 months, and 37.04%, 44.44% had conceived after treating them with dienogest followed by letrozole and letrozole and GnRH, for subsequent 3-6months, respectively. 13.64% , 36.36% , 50% of women had conceived spontaneously after laparoscopic ablation, after treating them with ablative procedure and letrozole and with letrozole and GnRH in the next 3-6 cycles, respectively. Spontaneous pregnancy and pregnancy following letrozole only or letrozole and GnRH in Group A and B were also not statistically significant (p - 0.961, p - 0.698).

Conclusion: Clinical pregnancy in infertile women with early endometriosis treated with dienogest is non-inferior to others treated with laparoscopic ablation and minimal adhesiolysis.

Introduction

The association between endometriosis and infertility is derived from various comparisons of fertile and infertile women, animal models, donor sperm studies, and assisted reproductive technique outcomes. Nearly 50% women of reproductive age group suffer from endometriosis and infertility [1]. However, the clinical presentations of endometriosis can vary widely, and many affected women are asymptomatic [2]. Diagnosis of endometriosis is quite a dilemma. Initially laparoscopy was gold standard diagnostic procedure, but it is invasive and now there has been a paradigm shift and diagnosis of endometriosis clinically and by ultrasonography has become a trend [3-6]. Hence non-invasive diagnostic tools and treatment is being considered and preferred now-a-days [7]. A careful discussion of potential risks involved with surgical

intervention, the balance of symptomatic relief, risks and complications of the procedure and recurrence should be explained to patients suffering from endometriosis and infertility. Dienogest is an oral progestin that has been investigated extensively recently, in the treatment of endometriosis, has showed a favorable safety and tolerability profile with predictable adverse effects, high rates of patient compliance, and low withdrawal rates [8]. If the disease is not arrested, or the diagnosis gets delayed patients face unfavourable consequences [9-11]. Endometriosis is a chronic, debilitating disease that affects approximately 10% of women of reproductive age, with a peak incidence in the age range of 25–30 years [12,13]. The aim of the present study was to compare the surgical management of mild and minimal endometriosis (rASRM) as compared to dienogest for limited period of time and subsequent fertility outcome.

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Materials and methods

A total of 150 woman aged range between 25-40 yr old who were referred to Department of Reproductive Medicine at Calcutta Fertility Mission, over a period of 36 months (January 2017 to December 2019) were enrolled in this retrospective observational study. 4 women were excluded as they had lost follow-up with us. The inclusion criteria were asymptomatic subfertile woman with early endometriosis, diagnosed clinically as well by transvaginal ultrasonography (TVUS) and laparoscopy. Women who had ovarian endometrioma, diagnosed adenomyosis, non-gynecological abdominal pain were excluded.

Work Plan

Out of a total of 146 women who were treated and followed up, 79 women satisfying the inclusion criteria were in Group A, who were prescribed Dienogest (2mg) for 3 months, following laparoscopy. 67 of the rest had undergone laparoscopy for unexplained infertility and were given ovulation induction, following the procedure. Laparoscopic ablation of the endometriotic lesions and correction of tubo-ovarian relation or minimal adhesiolysis, were done wherever necessary and the tissues were sent for histopathology for confirmation. The results in terms of clinical pregnancy rate (CPR) in subsequent 6 months were statistically analysed in both Groups A and B.

Ethical consideration

Institutional Ethical approval was obtained from the Ethics Committee of Calcutta Fertility Mission and verbal informed consent was obtained before the commencement of study.

Demographic and clinical information were obtained from prospective database on 11/03/2020 (code: CFM/2020/011).

Statistical analysis

Categorical variables are expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

Results

Discussion

In women with endometriosis desiring conception, case selection for laparoscopic ablation and minimal adhesiolysis is critical, and the surgical approach has to be individually tailored. Surgical intervention includes ablation of endometriotic lesions, cystectomy, and division of adhesions. Surgery is a quick procedure that can provide pain relief and enhances fertility, but this approach should be delayed, especially in infertility, for as long as possible due to the high risk of recurrence, which attains a rate of 40%–50% at five years. Recurrence after surgical intervention is common, while the clinical evidence to support the efficacy and safety of many medications currently used in endometriosis is limited [14]. Medications administered postoperatively may reduce the risk of recurrence. As per American Society for Reproductive Medicine, "Endometriosis should be viewed as a chronic disease that requires a life-long management plan

Table 1. Age of patients in both groups

		GROUP		Total	p Value	Significance
		GROUP A	GROUP B			
AGE in years	25-30	29(36.71)	20(29.85)	49(33.56)	0.657	Not Significant
	31-35	36(45.57)	35(52.24)	71(48.63)		
	36-40	14(17.72)	12(17.91)	26(17.81)		
Total		79(100)	67(100)	146(100)		

Data presented as n%, Pearson's Chi Square test for Independence of Attributes

Table 2. Comparison of clinical pregnancy rate with letrozole and gonadotropin in both groups

		GROUP		Total	p Value	Significance
		GROUP A	GROUP B			
PREGNANCY	SPONTANEOUS PREGNANCY*	5(18.52)	3(13.64)	8(16.33)	0.641	Not Significant
	PREGNANCY WITH LETROZOLE #	10(37.04)	8(36.36)	18(36.73)	0.961	Not Significant
	GONADOTROPIN AND LETROZOLE #	12(44.44)	11(50)	23(46.94)	0.698	Not Significant
Total		27(100)	22(100)	49(100)		

Data presented as n%

* Fisher's Exact Test

Pearson's Chi Square test for Independence of Attributes

with the goal of maximizing the use of medical treatment and avoiding repeated surgical procedures”[3]. Medical mode of management suppresses ovulation and hence there is a delay in pregnancy when infertility is concerned [3]. Different forms of medical treatment are advocated for endometriosis which causes pseudomenopause or pseudopregnancy. Moreover, previous literature have mentioned medical therapy does not improve the chance of spontaneous conception and should not be used as it is associated with considerable side effects [15]. On the other hand, surgical treatment of endometriosis is one-time procedure and attempt of pregnancy can be undertaken immediately after procedure. But there is a high chance of recurrence after surgical treatment of endometriosis. Though the latter is a fertility friendly treatment but disadvantage is its invasiveness and recurrence. In case of early endometriosis where tubo-ovarian relations are not much disturbed or there are no much pelvic adhesions, which may lead to so-called unexplained infertility, surgical treatment in the form of ablation or electro-coagulation of endometriotic spots might be more invasive. This probably adds to the biochemical ill-effect on infertility. On the contrary, dienogest has been successfully used to combat these lesions and pregnancy promotion can be conducted with ovulation induction, following the treatment for 90days. No organized compilation study of medical and surgical treatment for endometriosis causing infertility has yet been undertaken. In case of minimal and mild endometriosis; expectant treatment which is undertaken primarily yields some favourable result so far fertility is concerned, but outcome of medical treatment after diagnosis, is non-inferior to surgical treatment and expectant one, as presented in this study.

In patients with endometriosis, pretreatment with dienogest has proved to yield better oocyte retrieval, good blastocysts in patients and IVF outcome has also been seen to improve with dienogest. There are controversies regarding this when patients with moderate and severe endometriosis are taken into consideration, where no improvement is seen in clinical pregnancy outcome with administration of dienogest as pretreatment of IVF [16]. In our study 18.52% patients with early asymptomatic endometriosis, had conceived spontaneously after treatment with dienogest for 3 months and 37.04% had conceived after treating them with dienogest followed by letrozole for subsequent 3-6months. 44.44% women conceived after treatment with dienogest along with letrozole and GnRH in the next 3-6cycles. (Table 2) In patients with moderate and severe endometriosis surgical excision has been recommended as first line treatment. In those who failed to conceive spontaneously after surgery, assisted reproduction is more effective than repeat surgery. In women with minimal and mild endometriosis, surgical excision or ablation of endometriosis is also recommended as first line with doubling the pregnancy rate [17]. The present study shows 13.64% women had conceived spontaneously after laparoscopic ablation and 36.36% patients conceived after treating them with ablative procedure and letrozole in next 3-6 cycles.50% of women conceived after laparoscopic ablation along with letrozole and GnRH. Spontaneous clinical pregnancy following dienogest for 3 months and laparoscopic ablation in early endometriosis were almost similar (p value – 0.641). Pregnancy following letrozole only or letrozole and GnRH in Group A and B were also not statistically significant (p value -0.961, p value – 0.698

(Table 2). Hence we can conclude that clinical pregnancy in group of infertile women with early endometriosis treated with dienogest is non-inferior to the other group treated with laparoscopic ablation and minimal adhesiolysis.

Conflict of interest

There is no conflict of interest in between the authors involved in this study.

Acknowledgements

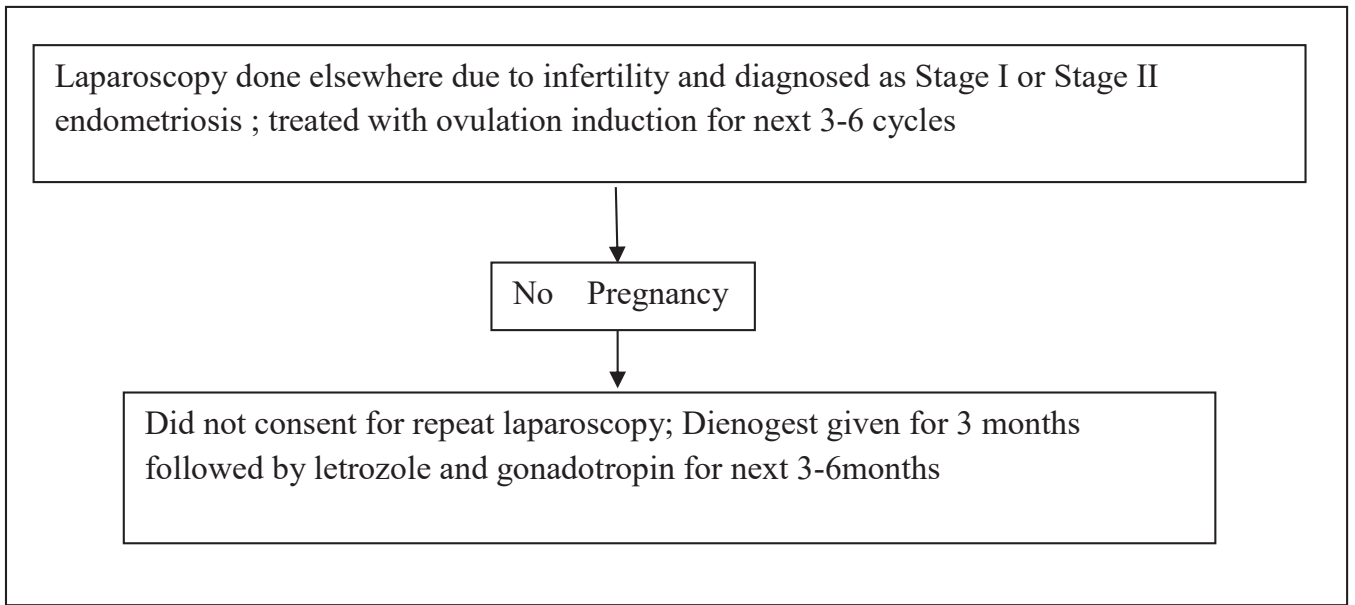
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References

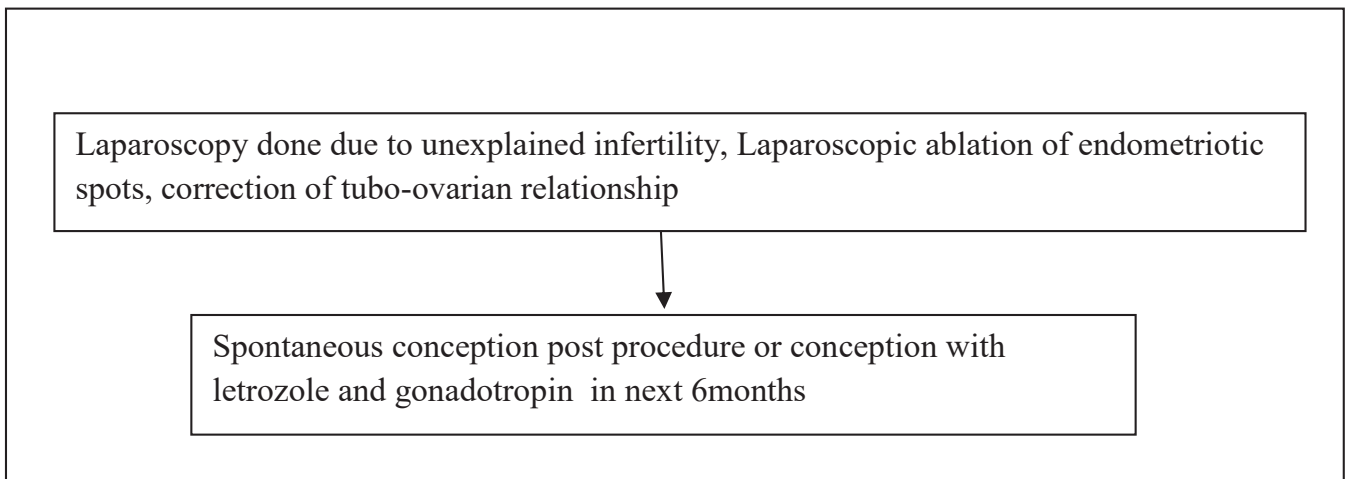
- Holoch KJ, Lessey BA. Endometriosis and infertility. Clin Obstet Gynecol. 2010;53(2):429–438.
- Schrager S, Falleroni J, Edgoose J. Evaluation and Treatment of Endometriosis. Am Fam Physician. 2013;87(2):107-113.
- Practice Committee of the American Society for Reproductive Medicine. Treatment of pelvic pain associated with endometriosis: a committee opinion. Fertil Steril. 2014;101(4):927-35.
- Leyland N, Casper R, Laberge P, Singh SS, SOGC. Endometriosis: diagnosis and management. J Obstet Gynaecol Can. 2010;32(2):1-32.
- Dunselman GA, Vermeulen N, Becker C, et al. ESHRE guideline: management of women with endometriosis. Hum Reprod. 2014 ;29(3):400-12.
- Johnson NP, Hummelshoj L, World Endometriosis Society Montpellier Consortium. Consensus on current management of endometriosis. Hum Reprod. 2013;28:1552-1568.
- Bagchi B, Siddhartha C, Arpan C. Finding a simplified clinical score for diagnosis and treatment of endometriosis without chocolate cyst. International Journal of Medical and Biomedical Studies. 2020; 4(4).
- Schindler AE. Dienogest in long-term treatment of endometriosis. Int J Womens Health. 2011;3:175-184.
- Nnoaham KE, Hummelshoj L, Webster P, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertil Steril. 2011;96(2):366-373.e8.
- Soliman AM, Fuldeore M, Snabes MC. Factors associated with time to endometriosis diagnosis in the United States. J Womens Health. 2017;26:788–97.
- Van der Zanden M, Teunissen DAM, Van der Woord IW, Braat DDM, Nelen WLD, Nap AW. Barriers and facilitators to the timely diagnosis of endometriosis in primary care in the Netherlands. Fam Pract. 2020;37(1):131-136.
- Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. J Assist Reprod Genet. 2010;27(8):441-447.
- Parasar P, Ozcan P, Terry KL. Endometriosis: Epidemiology, Diagnosis and Clinical Management. Curr Obstet Gynecol Rep. 2017;6(1):34-41.
- Selçuk I, Bozdağ G. Recurrence of endometriosis; risk factors, mechanisms and biomarkers; review of the literature. J Turk Ger Gynecol Assoc. 2013;14(2):98-103.
- Rafique S, Decherney AH. Medical Management of Endometriosis. Clin Obstet Gynecol. 2017;60(3):485-496.
- Barra, F, Antonio S L, Carolina S, Simone G, Fabio G, Simone F. Pretreatment with dienogest in women with endometriosis undergoing IVF after a previous failed cycle. Reproductive BioMedicine Online. 2020; 41(5):859 – 868.
- Rizk B, Turki R, Lotfy H, et al. Surgery for endometriosis-associated infertility: do we exaggerate the magnitude of effect? Facts Views Vis Obgyn. 2015;7(2):109-18.

SUPPLEMENTARY INFORMATION

Group A (79)



Group B (67)



Nos. of patients	Serial Number	Group A			Group B		
		Spontaneous pregnancy	Pregnancy with letrozole	Pregnancy with letrozole and GnRH	Spontaneous pregnancy	Pregnancy with letrozole	Pregnancy with letrozole and GnRH
1	CFM/17/211	Yes	NA	NA	NA	NA	NA
2	CFM/17/110	Yes	NA	NA	NA	NA	NA
3	CFM/17/111	Yes	NA	NA	NA	NA	NA
4	CFM/17/113	Yes	NA	NA	NA	NA	NA
5	CFM/17/115	Yes	NA	NA	NA	NA	NA
6	CFM/17/116	NA	Yes	NA	NA	NA	NA
7	CFM/17/119	NA	Yes	NA	NA	NA	NA
8	CFM/17/123	NA	Yes	NA	NA	NA	NA
9	CFM/17/127	NA	Yes	NA	NA	NA	NA
10	CFM/17/132	NA	Yes	NA	NA	NA	NA
11	CFM/17/133	NA	Yes	NA	NA	NA	NA
12	CFM/17/141	NA	Yes	NA	NA	NA	NA
13	CFM/18/151	NA	Yes	NA	NA	NA	NA
14	CFM/18/162	NA	Yes	NA	NA	NA	NA
15	CFM/18/163	NA	Yes	NA	NA	NA	NA
16	CFM/18/167	NA	NA	Yes	NA	NA	NA
17	CFM/18/169	NA	NA	Yes	NA	NA	NA
18	CFM/19/180	NA	NA	Yes	NA	NA	NA
19	CFM/19/183	NA	NA	Yes	NA	NA	NA
20	CFM/19/188	NA	NA	Yes	NA	NA	NA
21	CFM/19/189	NA	NA	Yes	NA	NA	NA
22	CFM/17/193	NA	NA	Yes	NA	NA	NA
23	CFM/17/197	NA	NA	Yes	NA	NA	NA
24	CFM/17/206	NA	NA	Yes	NA	NA	NA
25	CFM/17/211	NA	NA	Yes	NA	NA	NA
26	CFM/17/213	NA	NA	Yes	NA	NA	NA
27	CFM/17/215	NA	NA	Yes	NA	NA	NA
28	CFM/19/217	No	No	No	NA	NA	NA
29	CFM/19/231	No	No	No	NA	NA	NA
30	CFM/19/233	No	No	No	NA	NA	NA
31	CFM/19/239	No	No	No	NA	NA	NA
32	CFM/19/241	No	No	No	NA	NA	NA
33	CFM/19/244	No	No	No	NA	NA	NA
34	CFM/17/246	No	No	No	NA	NA	NA
35	CFM/17/255	No	No	No	NA	NA	NA
36	CFM/17/263	No	No	No	NA	NA	NA
37	CFM/17/271	No	No	No	NA	NA	NA
38	CFM/17/288	No	No	No	NA	NA	NA
39	CFM/17/293	No	No	No	NA	NA	NA
40	CFM/17/295	No	No	No	NA	NA	NA
41	CFM/17/311	No	No	No	NA	NA	NA
42	CFM/17/313	No	No	No	NA	NA	NA
43	CFM/19/317	No	No	No	NA	NA	NA
44	CFM/19/319	No	No	No	NA	NA	NA
45	CFM/19/322	No	No	No	NA	NA	NA

46	CFM/19/326	No	No	No	NA	NA	NA
47	CFM/19/328	No	No	No	NA	NA	NA
48	CFM/19/341	No	No	No	NA	NA	NA
49	CFM/19/355	No	No	No	NA	NA	NA
50	CFM/17/362	No	No	No	NA	NA	NA
51	CFM/17/372	No	No	No	NA	NA	NA
52	CFM/17/383	No	No	No	NA	NA	NA
53	CFM/17/116	No	No	No	NA	NA	NA
54	CFM/17/119	No	No	No	NA	NA	NA
55	CFM/17/123	No	No	No	NA	NA	NA
56	CFM/17/127	No	No	No	NA	NA	NA
57	CFM/18/138	No	No	No	NA	NA	NA
58	CFM/19/355	No	No	No	NA	NA	NA
59	CFM/19/367	No	No	No	NA	NA	NA
60	CFM/19/381	No	No	No	NA	NA	NA
61	CFM/17/392	No	No	No	NA	NA	NA
62	CFM/17/411	No	No	No	NA	NA	NA
63	CFM/18/146	No	No	No	NA	NA	NA
64	CFM/18/157	No	No	No	NA	NA	NA
65	CFM/18/161	No	No	No	NA	NA	NA
66	CFM/18/167	No	No	No	NA	NA	NA
67	CFM/18/169	No	No	No	NA	NA	NA
68	CFM/18/182	No	No	No	NA	NA	NA
69	CFM/18/195	No	No	No	NA	NA	NA
70	CFM/17/201	No	No	No	NA	NA	NA
71	CFM/17/215	No	No	No	NA	NA	NA
72	CFM/17/221	No	No	No	NA	NA	NA
73	CFM/17/237	No	No	No	NA	NA	NA
74	CFM/18/247	No	No	No	NA	NA	NA
75	CFM/18/254	No	No	No	NA	NA	NA
76	CFM/17/267	No	No	No	NA	NA	NA
77	CFM/17/276	No	No	No	NA	NA	NA
78	CFM/18/281	No	No	No	NA	NA	NA
79	CFM/18/302	NA	NA	NA	No	No	No
80	CFM/18/317	NA	NA	NA	No	No	No
81	CFM/18/391	NA	NA	NA	Yes	NA	NA
82	CFM/18/455	NA	NA	NA	Yes	NA	NA
83	CFM/18/432	NA	NA	NA	Yes	NA	NA
84	CFM/18/412	NA	NA	NA	NA	Yes	NA
85	CFM/18/401	NA	NA	NA	NA	Yes	NA
86	CFM/18/478	NA	NA	NA	NA	Yes	NA
87	CFM/18/347	NA	NA	NA	NA	Yes	NA
88	CFM/18/490	NA	NA	NA	NA	Yes	NA
89	CFM/18/434	NA	NA	NA	NA	Yes	NA
90	CFM/18/433	NA	NA	NA	NA	Yes	NA
91	CFM/18/458	NA	NA	NA	NA	Yes	NA
92	CFM/18/490	NA	NA	NA	NA	NA	Yes
93	CFM/18/387	NA	NA	NA	NA	NA	Yes

94	CFM/18/493	NA	NA	NA	NA	NA	Yes
95	CFM/18/473	NA	NA	NA	NA	NA	Yes
96	CFM/18/488	NA	NA	NA	NA	NA	Yes
97	CFM/18/512	NA	NA	NA	NA	NA	Yes
98	CFM/18/517	NA	NA	NA	NA	NA	Yes
99	CFM/18/531	NA	NA	NA	NA	NA	Yes
100	CFM/18/602	NA	NA	NA	NA	NA	Yes
101	CFM/18/645	NA	NA	NA	NA	NA	Yes
102	CFM/18/623	NA	NA	NA	NA	NA	Yes
103	CFM/18/604	NA	NA	NA	No	No	No
104	CFM/18/598	NA	NA	NA	No	No	No
105	CFM/18/567	NA	NA	NA	No	No	No
106	CFM/18/509	NA	NA	NA	No	No	No
107	CFM/18/543	NA	NA	NA	No	No	No
108	CFM/19/611	NA	NA	NA	No	No	No
109	CFM/19/677	NA	NA	NA	No	No	No
110	CFM/19/639	NA	NA	NA	No	No	No
111	CFM/19/671	NA	NA	NA	No	No	No
112	CFM/19/505	NA	NA	NA	No	No	No
113	CFM/19/661	NA	NA	NA	No	No	No
114	CFM/19/621	NA	NA	NA	No	No	No
115	CFM/19/611	NA	NA	NA	No	No	No
116	CFM/19/603	NA	NA	NA	No	No	No
117	CFM/19/661	NA	NA	NA	No	No	No
118	CFM/19/613	NA	NA	NA	No	No	No
119	CFM/19/609	NA	NA	NA	No	No	No
120	CFM/19/631	NA	NA	NA	No	No	No
121	CFM/19/674	NA	NA	NA	No	No	No
122	CFM/19/616	NA	NA	NA	No	No	No
123	CFM/19/690	NA	NA	NA	No	No	No
124	CFM/19/655	NA	NA	NA	No	No	No
125	CFM/19/601	NA	NA	NA	No	No	No
126	CFM/19/600	NA	NA	NA	No	No	No
127	CFM/19/592	NA	NA	NA	No	No	No
128	CFM/19/583	NA	NA	NA	No	No	No
129	CFM/19/689	NA	NA	NA	No	No	No
130	CFM/19/674	NA	NA	NA	No	No	No
131	CFM/18/688	NA	NA	NA	No	No	No
132	CFM/18/644	NA	NA	NA	No	No	No
133	CFM/18/619	NA	NA	NA	No	No	No
134	CFM/18/777	NA	NA	NA	No	No	No
135	CFM/18/745	NA	NA	NA	No	No	No
136	CFM/18/724	NA	NA	NA	No	No	No
137	CFM/18/719	NA	NA	NA	No	No	No
138	CFM/18/728	NA	NA	NA	No	No	No
139	CFM/18/701	NA	NA	NA	No	No	No
140	CFM/18/744	NA	NA	NA	No	No	No
141	CFM/18/713	NA	NA	NA	No	No	No

142	CFM/18/734	NA	NA	NA	No	No	No
143	CFM/19/733	NA	NA	NA	No	No	No
144	CFM/19/699	NA	NA	NA	No	No	No
145	CFM/19/622	NA	NA	NA	No	No	No
146	CFM/19/691	NA	NA	NA	No	No	No