

Application Number 21090

STATISTICAL REVIEW(S)

Statistical Review and Evaluation Clinical Studies

NDA #: 21-090/ _____ FEB 22 2000
Applicant: Organon Inc
Name of Drug: Cyclessa – CTR 77 (0.100/0.125/0.150 mg desogestrel/
0.025/0.025/0.025 mg ethinyl estradiol)
_____ - CTR 99 (0.050/0.125/0.150 mg desogestrel/
0.035/0.030/0.030 mg ethinyl estradiol)

Indication: Oral Contraception
Medical Reviewer: Daniel Davis, M.D.
Brenda Gierhart, M.D.
Statistical Reviewer: Moh-Jee Ng
Date of Submission: May 7, 1999 for 21-090
May 28, 1999 for 21-091

1. Introduction

The sponsor has presented the results of 2 clinical studies to establish the efficacy of CTR 77, and CTR 99 for prevention of pregnancy. CTR 77 and CTR 99 are 28-day oral contraceptives (OC). These studies compare CTR 77 and CTR 99 with a marketed drug, Ortho-Novum 7/7/7.

CTR 77 is a combination OC which contains 0.100/0.125/0.150 mg of DSG and 0.025/0.025/0.025 mg EE and CTR 99 contains 0.050/0.125/0.150 mg of DSG and 0.035/0.030/0.030 mg EE. These are to be administered in a 5/8/8 day regimen followed by 7 days of placebo. Ortho-Novum 7/7/7 contains 0.500/0.750/1.000 mg of NET and 0.035/0.035/0.035 mg EE to be administered in a 7/7/7 day regimen followed by 7 days of placebo.

CTR 77 is the subject of 21-090, and _____ Because the two NDAs included the same studies, this review will combine both NDAs.

2. Clinical Studies – 092001 and 092002

Studies 092001 and 092002 were conducted respectively in 65 and 67 centers in the US; each was an open-label, randomized, parallel group comparative, multicenter, safety and efficacy study (see Table 1).

The objectives of these studies were to evaluate the safety, contraceptive efficacy and cycle control compared with Ortho-Novum 7/7/7. Eligible women were randomized and received either CTR 77 or CTR 99 or Ortho-Novum 7/7/7 for 6 consecutive cycles. The studies required at least 10,000 cycles of exposure and at least 200 women completing a minimum of 6 months in treatment.

The treatment groups in each of the studies 092001 and 092002 were homogeneous with respect to demographic variables (age, race, and body mass index) and other subject characteristics (parity, smoking, and alcohol consumption).

Table 1
Summary of Studies 092001 and 092002

Study # Start/End Date	# Centers	Trial Design	Treatment & Dose	Subjects Enrolled/ Cycle of Exposure	Max. Cycles
092001 9/94 - 12/95	65	Open label, randomized, parallel group, comparative, multicenter, safety and efficacy	CTR 77 5 days - 0.100 mg DSG * 0.025 mg EE 8 days - 0.125 mg DSG * 0.025 mg EE 8 days - 0.150 mg DSG * 0.025 mg EE 7 days - Placebo	1392/7324	6 cycles 28-day cycles
			CTR 99 5 days - 0.050 mg DSG * 0.035 mg EE 8 days - 0.125 mg DSG * 0.030 mg EE 8 days - 0.150 mg DSG * 0.030 mg EE 7 days - Placebo	1387/7328	6 cycles 28-day cycles
			Ortho-Novum 7/7/7 7 days - 0.500 mg NET * 0.035 mg EE 7 days - 0.750 mg NET * 0.035 mg EE 7 days - 1.000 mg NET * 0.035 mg EE 7 days - Placebo	1393/7375	6 cycles 28-day cycles
092002 9/94 - 2/96	67	Open label, randomized, parallel group, comparative, multicenter, safety and efficacy	CTR 77 5 days - 0.100 mg DSG * 0.025 mg EE 8 days - 0.125 mg DSG * 0.025 mg EE 8 days - 0.150 mg DSG * 0.025 mg EE 7 days - Placebo	1376/7203	6 cycles 28-day cycles 6
			CTR 99 5 days - 0.050 mg DSG * 0.035 mg EE 8 days - 0.125 mg DSG * 0.030 mg EE 8 days - 0.150 mg DSG * 0.030 mg EE 7 days - Placebo	1389/7192	6 cycles 28-day cycles
			Ortho-Novum 7/7/7 7 days - 0.500 mg NET * 0.035 mg EE 7 days - 0.750 mg NET * 0.035 mg EE 7 days - 1.000 mg NET * 0.035 mg EE 7 days - Placebo	1391/7383	6 cycles 28-day cycles

3. Sponsor's Efficacy Results

Contraceptive effectiveness was based on the occurrence of pregnancy in the intent-to-treat (ITT) evaluation group. The ITT consists of subjects who took study drug with information on extent of exposure of study drug. However, due to problems with site 64/092002, the sponsor excluded this site from their analyses.

For the two studies combined, there were 23 pregnancies reported in the CTR 77 arm, 25 pregnancies in the CTR 99 arm, and 19 pregnancies in Ortho-Novum 7/7/7 (see Table 2):

- Pre-treatment pregnancies - those in which conception occurred prior to intake of study drug: 8 in CTR 77 and 8 in CTR 99
- In-treatment pregnancies - those in which conception occurred after the first tablet was taken and prior to discontinuation of the study drug: 12 from CTR 77 arm, 13 from CTR 99 arm, and 9 from Ortho-Novum 7/7/7
- Post-treatment pregnancies - those in which conception occurred after discontinuation of study drug: 3 in CTR 77, 4 in CTR 99, and 10 in Ortho-Novum 7/7/7

Table 2
Summary of all Pregnancies
Combined Studies

	CTR 77	CTR 99	Ortho-Novum 7/7/7
Pre-treatment pregnancies	8	8	0
In-treatment pregnancies	12	13	9
Post-treatment pregnancies	3	4	10
Total pregnancies	23	25	19

Pregnancy risk was estimated by the Pearl Index (Higgins and Wilkens, 1985) and by Life-Table Methods (Cutler and Ederer, 1958).

The Pearl Index is defined as the number of in-treatment pregnancies times 1300 divided by the total number of cycles of exposure. The Pearl Indices per 100 woman-years for study 092001 were 1.06 for CTR 77, 1.6 for CTR 99, and 1.06 for Ortho-Novum 7/7/7; and those for study 092002 were 1.08 for CTR 77, 0.72 for CTR 99, and 0.53 for Ortho-Novum 7/7/7. For the combined studies the indices were 1.08 for CTR 77, 1.17 for CTR 99, and 0.8 for Ortho-Novum 7/7/7 (see Table 3).

The Life-Table Method estimates the proportion of pregnancies in a fixed time period for the subject in-treatment pregnancies. The endpoint of interest was the six cycle cumulative probability of pregnancy. For study 092001, the life-table pregnancy rates were 0.005 for CTR 77, 0.0073 for CTR 99, and 0.0052 for Ortho-Novum 7/7/7. For study 092002, the life-table pregnancy rates were 0.0051 for CTR 77, 0.0034 for CTR 99, and 0.0025 for Ortho-Novum 7/7/7. For the combined studies the life-table pregnancy rates were 0.0051 for CTR 77, 0.0054 for CTR 99, and 0.0039 for Ortho-Novum 7/7/7 (see Table 3).

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Table 3
Sponsor's Efficacy Analyses
Excluding Site 64/092002
Intent-to-Treat Evaluation Group

	092001			092002			Combined Studies		
	CTR 77	CTR 99	Ortho- Novum 7/7/7	CTR 77	CTR 99	Ortho- Novum 7/7/7	CTR 77	CTR 99	Ortho- Novum 7/7/7
Total # of subjects	1,339	1,337	1,351	1,317	1,332	1,337	2,643	2,657	2675
Total cycle of exposures	7,329	7,334.4	7,362.7	7191.1	7191.6	7197.1	14,456	14,462.8	14,673.9
In-Treatment pregnancies	6	9	6	6	4	3	12	13	9
Pearl Index/100 women years	1.06	1.60	1.06	1.08	0.72	0.53	1.08	1.17	0.80
Life Table 6 months pregnancy rates	0.005	0.0073	0.0052	0.0051	0.0034	0.0025	0.0051	0.0054	0.0039

4. Reviewer's Analyses

This reviewer's analyses are based on the ITT evaluation group from the sponsor's data sets submitted on August 5, 1999. This reviewer confirmed the Pearl Index and Life Table Pregnancies rates obtained by the sponsor. However, due to problems with site 12/092002, the medical reviewer, Dr. Gierhart, requested exclusion of this site from the analyses. One in-treatment pregnancy for each of the CTR 77 and CTR 99 groups of study 092002 at site 12 was excluded from this reviewer's analyses, reducing the number of in-treatment pregnancies from 12 to 11 for CTR 77, and from 13 to 12 for CTR 99.

This reviewer used SAS PROC LIFETEST procedure to estimate the pregnancy rate at the end of cycle 6 based on the data provided by the sponsor. Pregnancy Odds Ratios and Life Table Pregnancy Rates with 95% confidence intervals were calculated. The confidence intervals for the odds ratios were adjusted for two multiple comparison with the control arm, using a Bonferroni correction. Efficacy results are summarized in Table 4.

Further analyses were done by this reviewer to include pregnancies conceived less than 28 days after discontinuation of study drug. An additional 13 pregnancies were included; 1 from CTR 77, 4 from CTR 99 and 8 from Ortho-Novum 7/7/7. See Table 4 for the Pearl Index results and Tables 5-7 for the Life-Table Pregnancy Rate results.

This review also analyzed pregnancies conceived less than 14 days after discontinuation of study drug (see attachment). In addition, this reviewer analyzed pregnancies conceived less than 7 days after discontinuation of study drug; the results were essentially identical to the analyses of the in-treatment pregnancies.

Table 4
Reviewer's Efficacy Analyses
Excluding Sites 12/092002 and 64/092002
Intent-to-Treat Evaluation Group

	092001			092002			Combined Studies		
Pregnancies conceived on study drug									
	CTR 77	CTR 99	Ortho-Novum 7/7/7	CTR 77	CTR 99	Ortho-Novum 7/7/7	CTR 77	CTR 99	Ortho-Novum 7/7/7
Total # of subjects	1,338	1,336	1,353	1,259	1,272	1,277	2,579	2,585	2,606
Total cycle of exposures	7,323.61	7,328.43	7,374.68	6,874.61	6,856.57	7,046.43	14,198.21	14,062.11	14,293.89
In-Treatment pregnancies	6	9	6	5	3	3	11	12	9
Pearl Index/100 women years	1.07	1.60	1.06	0.95	0.57	0.55	1.0	1.11	0.82
Odds ratios (97.5% CI) relative to Ortho Novum 7/7/7	1.01 (0.28,2.7)	1.52 (0.47,4.98)	-	1.69 (0.33,8.72)	1.0 (0.16,6.27)	-	1.24 (0.45,3.39)	1.35 (0.5,3.62)	-
Life Table 6 months pregnancy rates (95% CI)	0.004 (0.0005,0.008)	0.007 (0.003,0.01)	0.005 (0.001,0.009)	0.004 (0.0005,0.008)	0.003 (-0.0003,0.006)	0.003 (-0.0003,0.006)	0.005 (0.002,0.007)	0.006 (0.002,0.008)	0.004 (0.001,0.006)
Pregnancies conceived while on study drug and pregnancies conceived less than 28 days after discontinuation of study drug									
# pregnancies	6	10	10	6	6	7	12	16	17
Pearl Index/100 women years	1.07	1.77	1.76	1.13	1.14	1.29	1.10	1.48	1.55
Odds ratios (97.5% CI) relative to Ortho Novum 7/7/7	0.6 (0.19,1.93)	1.01 (0.37,2.78)	-	0.87 (0.25,3.03)	0.86 (0.25,3.0)	-	0.71 (0.31,1.67)	0.95 (0.43,2.08)	-
Life Table 6 months pregnancy rates (95% CI)	0.05 (-.04,0.01)	0.06 (-.04,0.2)	0.008 (0.003,0.01)	0.006 (0.002,0.01)	0.06 (-.02,0.1)	0.1 (-.004,0.2)	0.03 (-.03,0.07)	0.06 (-.003,0.1)	0.06 (0.0007,0.1)

Table 5
Pregnancy Rate
Study 092001

	CTR 77			CTR 99			Ortho-Novum 7/7/7		
Cycle	# subj entering	# preg	Pregnancy rate with 95% CI	# subj entering	# preg	Pregnancy rate with 95% CI	# subj entering	# preg	Pregnancy rate with 95% CI
Pregnancies conceived while on study drug									
1	1337	0	0.	1334	2	0.002 (-.0006,0.004)	1352	0	0.
2	1273	1	0.0008 (-.0008, 0.003)	1288	1	0.003 (-.0003, 0.005)	1294	0	0.
3	1239	1	0.002 (-0.0006,0.004)	1246	2	0.004 (0.0005,0.008)	1245	0	0.
4	1195	3	0.004 (0.0006,0.008)	1192	2	0.006 (0.001,0.01)	1200	2	0.002 (-.0006,0.004)
5	1177	0	0.004 (0.0006,0.008)	1171	2	0.007 (0.003,0.01)	1182	0	0.002 (-.0006,0.004)
6	1158	0	0.004 (0.0006,0.008)	1149	0	0.007 (0.003,0.01)	1157	4	0.005 (-.001,0.009)
Pregnancies conceived while on study drug and pregnancies conceived less than 28 days after discontinuation of study drug									
1	1337	0	0.	1334	2	0.002 (-.0006,0.004)	1352	0	0.
2	1273	1	0.0008 (-.0008, 0.003)	1288	1	0.003 (-.0003, 0.005)	1294	0	0.
3	1239	1	0.002 (-0.0006,0.004)	1246	2	0.004 (0.0005,0.008)	1245	2	0.002 (-.0006,0.004)
4	1195	3	0.004 (0.0006,0.008)	1192	2	0.006 (0.001,0.01)	1200	2	0.003 (.00007,0.006)
5	1177	0	0.004 (0.0006,0.008)	1171	2	0.007 (0.003,0.01)	1182	2	0.005 (0.001,0.009)
6	1158	0	0.004 (0.0006,0.008)	1149	0	0.007 (0.003,0.01)	1157	4	0.008 (0.003,0.01)
7	21	1	0.05 (-.04,0.1)	18	1	0.06 (-.04,0.17)			

Table 6
Pregnancy Rate
Study 092002

	CTR 77			CTR 99			Ortho-Novum 7/7/7		
Cycle	# subj entering	# preg	Pregnancy rate with 95% CI	# subj entering	# preg	Pregnancy rate with 95% CI	# subj entering	# preg	Pregnancy rate with 95% CI
Pregnancies conceived while on study drug									
1	1258	1	0.0008 (-.0008, 0.003)	1270	1	0.0008 (-.0008, 0.003)	1276	0	0.
2	1204	0	0.0008 (-.0008, 0.003)	1212	0	0.0008 (-.0008, 0.003)	1230	0	0.
3	1166	0	0.0008 (-.0008, 0.003)	1271	1	0.002 (-.0006, 0.004)	1195	0	0.
4	1118	3	0.003 (0.00007, 0.007)	1111	0	0.002 (-.0006, 0.004)	1152	2	0.002 (-.0007,0.005)
5	1097	1	0.004 (0.0005, 0.008)	1091	0	0.002 (-.0006, 0.004)	1131	0	0.002 (-.0007,0.005)
6	1080	0	0.004 (0.0005, 0.008)	1064	1	0.003 (-.0003, 0.006)	1111	1	0.003 (-.00031,0.006)
Pregnancies conceived while on study drug and pregnancies conceived less than 28 days after discontinuation of study drug									
1	1258	1	0.0008 (-.0008, 0.003)	1270	1	0.0008 (-.0008, 0.003)	1276	0	0.
2	1204	1	0.0008 (-.0006, 0.004)	1212	0	0.0008 (-.0008, 0.003)	1230	0	0.
3	1166	0	0.0008 (-.0006, 0.004)	1271	2	0.003 (-.00003, 0.006)	1195	0	0.
4	1118	2	0.003 (0.00007, 0.006)	1111	0	0.003 (-.00003, 0.006)	1152	2	0.002 (-.0007,0.005)
5	1097	3	0.006 (0.002, 0.01)	1091	0	0.003 (-.00003, 0.006)	1131	0	0.002 (-.0007,0.005)
6	1080	0	0.006 (0.002, 0.01)	1064	1	0.003 (0.00007,0.007)	1111	2	0.004 (.00008,0.007)
7				34	2	0.06 (-.017,0.1)	30	3	0.1 (-.004,1.2)

Table 7
Pregnancy Rate
Combined Studies

Cycle	CTR 77			CTR 99			Ortho-Novum 7/7/7		
	# subj entering	# preg	Pregnancy rate with 95% CI	# subj entering	# preg	Pregnancy rate with 95% CI	# subj entering	# preg	Pregnancy rate with 95% CI
Pregnancies conceived while on study drug									
1	2596	1	0.0004 (-.00003,0.001)	2605	3	0.001 (-.0002,0.003)	2629	0	0.
2	2478	1	0.0007 (-.00003, 0.003)	2504	1	0.002 (.00003, 0.003)	2525	0	0.
3	2406	1	0.001 (-0.0002,0.003)	2417	3	0.003 (0.0007,0.005)	2442	0	0.
4	2313	5	0.003 (0.001,0.006)	2304	1	0.003 (0.001,0.006)	2352	4	0.002 (.00004,0.003)
5	2275	2	0.004 (0.002,0.007)	2263	3	0.005 (0.002,0.007)	2314	0	0.002 (.00004,0.003)
6	2240	0	0.004 (0.002,0.007)	2215	1	0.005 (0.003,0.008)	2268	5	0.004 (.001,0.006)
Pregnancies conceived while on study drug and pregnancies conceived less than 28 days after discontinuation of study drug									
1	2596	1	0.0004 (-.00003,0.001)	2605	3	0.001 (-.0002,0.003)	2629	0	0.
2	2478	2	0.001 (-.00002, 0.003)	2504	1	0.002 (.00003, 0.003)	2525	0	0.
3	2406	1	0.002 (0.000003,0.003)	2417	4	0.003 (0.001,0.005)	2442	2	0.0008 (-.0003,0.002)
4	2313	5	0.004 (0.001,0.006)	2304	1	0.004 (0.001,0.006)	2352	4	0.003 (.00005,0.004)
5	2275	2	0.005 (0.002,0.007)	2263	3	0.005 (0.002,0.008)	2314	2	0.003 (.001,0.006)
6	2240	0	0.005 (0.002,0.007)	2215	1	0.005 (0.002,0.008)	2268	6	0.006 (.003,0.009)
7	48	1	0.03 (-0.01,0.07)	7	3	0.06 (-.0003,0.1)	58	3	0.06 (0.0007,0.1)

5. Review's Conclusion and Comments

These reviewer efficacy analyses of the Pearl Index and the Life-Table Pregnancy Rate are consistent with those of the sponsor's for both studies and the combined studies. However, for study 092002, after deleting site 12 at the request of the medical reviewer, the Pearl Index decreased from 1.08 to 0.95 for CTR 77, 0.72 to 0.57 for CTR 99, and remained about the same (0.53 to 0.55) for Ortho-Novum 7/7/7. The pregnancy rates decreased from 0.0051 to 0.004 for CTR 77, from 0.0034 to 0.003 for CTR 99, and remained about the same (0.0025 to 0.003) for Ortho-Novum 7/7/7.

Further, after including pregnancies conceived less than 28 days after discontinuation of study drug, the number of pregnancies increased from 11 to 12 for CTR 77, from 12 to 16 for CTR 99, and from 9 to 17 for Ortho-Novum 7/7/7 in the combined studies (see Table 4). The pregnancy odds ratios relative to Ortho-Novum 7/7/7 decreased in both studies and the combined studies while the Pearl Index increased for each treatment group (see Table 4).


 Moh-Jee Ng, M.S.
 Mathematical Statistician
 2/18/2000

Concur: Lisa Kammerman, Ph.D. *LK 2/18/00*

Ed Nevius, Ph.D. *EN 2/22/00*

cc: Original NDA 21-090/
HFD-580/ Division file
HFD-580/Daniel Davis, M.D.
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HFD-580/Jennifer Mercier, B.S.
HFD-715/ENevius, LKammerman, MNg

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**Number of Pages
Redacted** 3



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Attachment

Reviewer's Additional Efficacy Analyses
Pregnancies conceived while on study drug and pregnancies conceived
less than 14 days after discontinuation of study drug

	092001			092002			Combined Studies		
	CTR 77	CTR 99	Ortho-Novum 777	CTR 77	CTR 99	Ortho-Novum 777	CTR 77	CTR 99	Ortho-Novum 777
Total # of subjects	1,338	1,336	1,353	1,259	1,272	1,277	2,579	2,585	2,606
Total cycle of exposures	7,323.61	7,328.43	7,374.68	6,874.61	6,856.57	7,046.43	14,198.21	14,062.11	14,293.89
# pregnancies	6	9	8	5	3	7	11	12	15
Pearl Index/100 women years	1.07	1.60	1.41	0.95	0.57	1.29	1.0	1.11	1.36
Odds ratios (97.5% CI) relative to Ortho Novum 777	0.76 (0.23,2.55)	1.14 (0.38,3.4)	-	0.72 (0.19,2.7)	0.43 (0.09,2.02)	-	0.74 (0.3,1.8)	0.81 (0.34,1.92)	-
Life Table 6 months pregnancy rates (95%CI)	0.005 (0.001,0.008)	0.007 (0.003,0.01)	0.007 (0.002,0.01)	0.004 (0.0005,0.008)	0.003 (-0.0003,0.006)	0.1 (-0.004,0.2)	0.005 (0.002,0.007)	0.006 (0.002,0.008)	0.005 (0.002,0.008)

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**Filing Meeting
Division of Biometrics II**

JUN 29 1999

NDA #: 21-090
Sponsor: Organon Inc
Indication: Oral Contraception
Code Name: CTR 77
Generic Name: desogestrel (DSG) and ethinyl estradiol (EE) Tablets
Strengths: 0.100/0.125/0.150 mg DSG and 0.025/0.025/0.025 mg EE
No. of Controlled Studies: 2 clinical studies
Date of Submission: May 7, 1999
Date of 45 Day Meeting: June 26, 1999
User Fee Goal Date: March 7, 2000
User Fee Date: May 7, 2000
Anticipated Review Completion Date: February 14, 2000
Volume numbers in statistical section: 1.1, 1.3, 1.49, 1.56, 1.69, 1.77 and 1.101
Screened by: Moh-Jee Ng

CHECKLIST

Item	Yes	No
Index sufficient to locate necessary reports, tables, etc.	√	
Original protocols & subsequent amendments available in the NDA	√	
Designs utilized appropriate for the indications requested	√	
Endpoints and methods of analysis spelled out in the protocols	√	
Interim analyses (If present) planned in the protocol and appropriate adjustments in significance level made	NA	
Appropriate references included for novel statistical methodology (if present)		√
Sufficient data listings and intermediate analysis tables to permit a statistical review	√	
Data from primary studies on diskettes and/or CANDAs submitted		√
Intent-to-treat analyses	√	
Effects of dropouts on primary analyses investigated	√	
Safety and efficacy for gender, racial, and geriatric subgroups investigated		√

Summary of all Clinical Trials

Study # Start/End Date	# Centers	Trial Design	Treatment & Dose	Subjects Enrolled/ Cycle of Exposure	Max. Cycles	Volumes
092001 9/94 - 12/95	65	Open label, randomized, parallel group, comparative, multicenter, safety and efficacy	CTR 99 5 days - 0.050 mg DSG * 0.035 mg EE 8 days - 0.125 mg DSG * 0.030 mg EE 8 days - 0.150 mg DSG * 0.030 mg EE 7 days - Placebo	1387/7328	6 cycles	1.49 - 1.68
			CTR 77 7 days - 0.100 mg DSG * 0.025 mg EE 7 days - 0.125 mg DSG * 0.025 mg EE 7 days - 0.150 mg DSG * 0.025 mg EE 7 days - Placebo	1392/7324	6 cycles	
			Ortho-Novum 7/7/7 7 days - 0.500 mg DSG * 0.035 mg EE 7 days - 0.750 mg DSG * 0.035 mg EE 7 days - 1.000 mg DSG * 0.035 mg EE 7 days - Placebo	1393/7375		
092002 9/94 - 2/96	67	Open label, randomized, parallel group, comparative, multicenter, safety and efficacy	CTR 99 5 days - 0.050 mg DSG * 0.035 mg EE 8 days - 0.125 mg DSG * 0.030 mg EE 8 days - 0.150 mg DSG * 0.030 mg EE 7 days - Placebo	1389/7192	6 cycles	1.69 - 1.90
			CTR 77 7 days - 0.100 mg DSG * 0.025 mg EE 7 days - 0.125 mg DSG * 0.025 mg EE 7 days - 0.150 mg DSG * 0.025 mg EE 7 days - Placebo	1376/7203	6 cycles	
			Ortho-Novum 7/7/7 7 days - 0.500 mg DSG * 0.035 mg EE 7 days - 0.750 mg DSG * 0.035 mg EE 7 days - 1.000 mg DSG * 0.035 mg EE 7 days - Placebo	1391/7383		

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