Effects on Hemostasis, Lipids, Carbohydrate Metabolism, Adrenal & Thyroid Function of the Combined Oral Contraceptive NOMAC-E2 Compared to a COC Containing LNG-EE (292004)(COMPLETED)(P05764)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00511355

First received: August 2, 2007
Last updated: November 14, 2014
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History of Changes

Purpose

The primary purpose of this study is to evaluate the effects of the combined oral contraceptive (COC) NOMAC-E2 on hemostasis, lipids, carbohydrate metabolism, adrenal function, and thyroid function.

Condition	Intervention	Phase
Contraception	Drug: NOMAC-E2 Drug: Levonorgestrel and Ethinyl Estradiol	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Prevention

Official Title: A Randomized, Open-Label, Comparative, Multi -Center Trial to Evaluate the Effects on Hemostasis, Lipids and Carbohydrate Metabolism, and on Adrenal and Thyroid Function of a Monophasic COC Containing 2.5 mg NOMAC and 1.5 mg E2 Compared to a Monophasic COC Containing 150 ug LNG and 30 ug EE

Resource links provided by NLM:

MedlinePlus related topics: Thyroid Diseases

Drug Information available for: Estradiol Ethinylestradiol Estradiol cypionate Levonorgestrel Estradiol valerate Estradiol acetate Estradiol hemihydrate

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Serum Concentration of Prothrombin Fragments 1 + 2 [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of D-Dimer [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Activated Protein C (APC) Resistance Ratio (Endogenous Thrombin Potential [ETP]-Based) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). APC resistance ratio (ETP-based) measures the anticoagulation response of plasma to APC after activation of the extrinsic coagulation pathway. An increase in the ratio indicates a reduced responsiveness to APC. Each cycle consists of 28 days.

- Serum Concentration of Clotting Factor VIIa [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Clotting Factor VIIc [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Clotting Factor VIII [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Clotting Factor II [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Antithrombin III [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Protein S (Free) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Protein S (Total) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Protein C [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle

consists of 28 days.

- APC Resistance Ratio (Activated Partial Thromboplastin Time [APTT]-Based) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). APC resistance ratio (APTT-based) measures the anticoagulation response of plasma to APC after activation of the intrinsic coagulation pathway. An increase in the ratio indicates a increased responsiveness to APC. Each cycle consists of 28 days.

- Serum Concentration of Sex Hormone Binding Globulin (SHBG) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of C-Reactive Protein (CRP) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Total Cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of High Density Lipoprotein (HDL)-Cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of HDL2-cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of HDL3-cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Low Density Lipoprotein (LDL)-Cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Apolipoprotein A-1 [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Apolipoprotein B [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Lipoprotein(a) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle

consists of 28 days.

- Serum Concentration of Total Triglycerides [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Area Under the Curve Over 3 Hours (AUC3) for Glucose (Oral Glucose Tolerance Test [OGTT]) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Blood glucose levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Each cycle consists of 28 days.

- Incremental AUC3 for Glucose (OGTT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Blood glucose levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Incremental area under the curve was defined as incremental AUC3 = AUC3 - 3*fasting concentration. Each cycle consists of 28 days.

- AUC3 for Insulin (OGTT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Blood insulin levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Each cycle consists of 28 days.

- Incremental AUC3 for Insulin (OGTT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Blood insulin levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Incremental area under the curve was defined as incremental AUC3 = AUC3 - 3*fasting concentration. Each cycle consists of 28 days.

- Serum Concentration of Hemoglobin Type A1c (HbA1c) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). HbA1c was determined before glucose loading. Each cycle consists of 28 days.

- Serum Concentration of Total Cortisol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Corticosteroid Binding Globulin (CBG) [Time Frame: Baseline to Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Thyroid Stimulating Hormone (TSH) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Free Thyroxine (T4) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Thyroxin Binding Globulin (TBG) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

Secondary Outcome Measures:

- Serum Concentration of Total Testosterone [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Free Testosterone [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Dehydroepiandrosterone Sulphate (DHEAS) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Androstenedione [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Serum Concentration of Dihydrotestosterone (DHT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)] [Designated as safety issue: Yes]

  Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

- Number of In-treatment Pregnancies (With +2 Day Window) Per 100 Woman Years of Exposure (Pearl Index) [Time Frame: 6 cycles] [Designated as safety issue: No]

  In-treatment pregnancies were pregnancies with an estimated date of conception from the day of first intake of trial medication up to and including the day of last (active or placebo) intake of trial medication extended with a maximum of 2 days. Each 13 cycles (28 days per cycle) constitutes a woman year. The Pearl Index was obtained by dividing the number of in-treatment pregnancies that occurred by the time (in 100 women years) that the women were under risk of becoming pregnant.

- Number of Participants With an Occurrence of Breakthrough Bleeding/Spotting [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough bleeding/spotting was defined as any episode that occurred during the "expected non-bleeding period" that was neither an early nor a continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.

- Number of Participants With an Occurrence of Absence of Withdrawal Bleeding [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Absence of withdrawal bleeding was defined as no bleeding/spotting episode that began during or continued into the "expected bleeding period". Expected bleeding period: NOMAC-E2: 7-day period starting on Day 25 of the cycle and ending on Day 3 of the next cycle; LNG-EE: 7-day period starting on Day 22 of the cycle.

- Number of Participants With an Occurrence of Breakthrough Bleeding [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants

documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough bleeding was defined as any bleeding episode that occurred during the "expected non-bleeding period" that was neither part of an early nor continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.

- Number of Participants With an Occurrence of Breakthrough Spotting (Spotting Only) [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough spotting was defined as any spotting episode that occurred during the "expected non-bleeding period" that was neither part of an early nor continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.

- Number of Participants With an Occurrence of Early Withdrawal Bleeding [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Early withdrawal bleeding was defined as any withdrawal bleeding that started before the current "expected bleeding period". Expected bleeding period: NOMAC-E2: 7-day period starting on Day 25 of the cycle and ending on Day 3 of the next cycle; LNG-EE: 7-day period starting on Day 22 of the cycle.

- Number of Participants With an Occurrence of Continued Withdrawal Bleeding [Time Frame: Every 28-day cycle for 5 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Continued withdrawal bleeding was defined as any withdrawal bleeding that continued into the "expected non-bleeding period" of the next cycle. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.

- Average Number of Breakthrough Bleeding/Spotting Days [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough bleeding/spotting was defined as any episode that occurred during the "expected non-bleeding period" that was neither an early nor a continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.

- Average Number of Withdrawal Bleeding/Spotting Days [Time Frame: Every 28-day cycle for 6 cycles] [Designated as safety issue: No]

  Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Withdrawal bleeding/spotting was defined as any episode that occurred during the "expected bleeding period". Expected bleeding period: NOMAC-E2: 7-day period starting on Day 25 of the cycle and ending on Day 3 of the next cycle; LNG-EE: 7-day period starting on Day 22 of the cycle.

Enrollment:	121
Study Start Date:	September 2006
Study Completion Date:	January 2008
Primary Completion Date:	January 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: NOMAC-E2 Nomegestrol Acetate (NOMAC) and Estradiol (E2), 2.5 mg NOMAC and 1.5 mg E2 monophasic combined oral contraceptive	Drug: NOMAC-E2 Nomegestrol Acetate and Estradiol (NOMAC-E2) Tablets, 2.5 mg NOMAC and 1.5 mg E2 taken once daily from Day 1 of menstrual period up to and including Day 28 for 6 consecutive 28-day cycles. Other Names: • SCH 900121 • Org 10486-0 (NOMAC) • Org 2317 (E2)

Active Comparator: LNG-EE Levonorgestrel and Ethinyl Estradiol Tablets (LNG-EE), 150 mcg LNG and 30 mcg EE	Drug: Levonorgestrel and Ethinyl Estradiol Levonorgestrel and Ethinyl Estradiol (LNG-EE) Tablets, 150 mcg LNG and 30 mcg EE taken once daily from Day 1 of menstrual period up to and including Day 28 for 6 consecutive 28-day cycles.

Eligibility

Ages Eligible for Study: 18 Years to 50 Years
Genders Eligible for Study: Female
Accepts Healthy Volunteers: Yes

Criteria

Inclusion Criteria:

- Sexually active women, at risk for pregnancy and not planning to use during trial medication use;
- Women in need for contraception and willing to use an oral contraceptive (OC) for 6 months (6 cycles);
- At least 18 but not older than 50 years of age at the time of screening;
- Body mass index = 17 and = 29 kg/m^2;
- Good physical and mental health;
- Willing to give informed consent in writing

Exclusion Criteria:

- Present use or use within 2 months prior to screening of any other hormonal treatment including sex hormones (other than contraceptives), insulin, thyroid and corticosteroid hormones (with the exception for local dermatological use);
- Contraindications for contraceptive steroids
- Presence or history (within 1 year before screening) of alcohol or drug abuse as judged by the (sub)investigator.
- An abnormal cervical smear (i.e.: dysplasia, cervical intraepithelial neoplasia [CIN], SIL, carcinoma in situ, invasive carcinoma) at screening or documentation of an abnormal smear performed within 6 months before screening;
- Clinically relevant abnormal laboratory result at screening as judged by the (sub) investigator;
- Use of an injectable hormonal method of contraception prior to screening; within 6 months of an injection with a 3 -month duration, within 4 months to screening of an injection with a 2-month duration, within 2 months of an injection with a 1-month duration;
- Before spontaneous menstruation has occurred following a delivery or abortion;
- Breastfeeding or within 2 months after stopping breastfeeding prior to the start of trial medication;
- Present use or use within 2 months prior to the start of the trial medication of the following drugs: phenytoin, barbiturates, primidone, carbamazepine, oxcarbazepine, topiramate, felbamate, rifampicin, nelfinavir, ritonavir, griseofulvin, ketoconazole, lipid-lowering drugs, anticoagulants and herbal remedies containing Hypericum perforatum (St John's Wort);
- Use of pharmacological agents which affect the hemostatic system during the pretreatment blood sampling: vitamin K (only prohibited within two weeks prior to sampling), nonsteroidal anti-inflammatory drugs (NSAIDS) and aspirin (both only prohibited during the week prior to sampling);
- Administration of investigational drugs and/or participation in another clinical trial within 2 months prior to the start of the trial medication or during the trial period.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

No Contacts or Locations Provided

More Information

Publications:

Ågren UM, Anttila M, Mäenpää-Liukko K, Rantala ML, Rautiainen H, Sommer WF, Mommers E. Effects of a monophasic combined oral contraceptive containing nomegestrol acetate and 17β-oestradiol compared with one containing levonorgestrel and ethinylestradiol on

haemostasis, lipids and carbohydrate metabolism. Eur J Contracept Reprod Health Care. 2011 Dec;16(6):444-57. doi: 10.3109/13625187.2011.604450.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00511355 History of Changes
Other Study ID Numbers:	P05764 Organon Protocol No. 292004
Study First Received:	August 2, 2007
Results First Received:	July 28, 2011
Last Updated:	November 14, 2014
Health Authority:	Finland: Finnish Medicines Agency

Additional relevant MeSH terms:

Contraceptives, Oral	Contraceptive Agents
Contraceptives, Oral, Combined	Contraceptive Agents, Female
Estradiol	Contraceptives, Oral, Synthetic
Estradiol 17 beta-cypionate	Estrogens
Estradiol 3-benzoate	Hormones
Estradiol valerate	Hormones, Hormone Substitutes, and Hormone Antagonists
Ethinyl Estradiol	Pharmacologic Actions
Ethinyl estradiol, levonorgestrel drug combination	Physiological Effects of Drugs
Levonorgestrel	Reproductive Control Agents
Polyestradiol phosphate	Therapeutic Uses

ClinicalTrials.gov processed this record on May 08, 2016

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Effects on Hemostasis, Lipids, Carbohydrate Metabolism, Adrenal & Thyroid Function of the Combined Oral Contraceptive NOMAC-E2 Compared to a COC Containing LNG-EE (292004)(COMPLETED)(P05764)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00511355

First received: August 2, 2007
Last updated: November 14, 2014
Last verified: November 2014
History of Changes

Results First Received: July 28, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Prevention
Condition:	Contraception
Interventions:	Drug: NOMAC-E2 Drug: Levonorgestrel and Ethinyl Estradiol

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description

NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Participant Flow: Overall Study

	NOMAC-E2	LNG-EE
STARTED	**60**	**61**
COMPLETED	**53**	**52**
NOT COMPLETED	**7**	**9**
Adverse Event	**4**	**4**
Pregnancy Wish	**1**	**0**
Lost to Follow-up	**2**	**1**
Other Reason	**0**	**1**
Pre-treatment (serious) adverse event	**0**	**1**
Withdrawal of informed consent	**0**	**1**
Other reason pre-treatment	**0**	**1**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
NOMAC-E2	All-participants-treated group. Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles
LNG-EE	All-participants-treated group. Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28, placebo tablets) for 6 consecutive 28-day cycles
Total	Total of all reporting groups

Baseline Measures

	NOMAC-E2	LNG-EE	Total
Number of Participants [units: participants]	60	58	118
Age [1] [units: years] Mean (Standard Deviation)	28.2 (8.2)	29.1 (7.8)	28.7 (8.0)
Gender [1] [units: participants]			
Female	60	58	118
Male	0	0	0

[1] All-participants-treated group. For the LNG-EE arm, this population excludes 3 subjects who were randomized but not treated.

Outcome Measures

Hide All Outcome Measures

1. Primary: Serum Concentration of Prothrombin Fragments 1 + 2 [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Prothrombin Fragments 1 + 2
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed	60	58

[units: participants]		
Serum Concentration of Prothrombin Fragments 1 + 2 **[units: nmol/L]** **Mean (Standard Deviation)**		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**0.18 (0.20)**	**0.19 (0.08)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**0.31 (1.06)**	**0.42 (1.17)**

Statistical Analysis 1 for Serum Concentration of Prothrombin Fragments 1 + 2

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0849

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

2. Primary: Serum Concentration of D-Dimer [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of D-Dimer
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg

	ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of D-Dimer [units: mg/L Fibrinogen Equivalent Units (FEU)] Mean (Standard Deviation)		
Baseline (n=60; NOMAC-E2; n=58)	**0.21 (0.16)**	**0.19 (0.14)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**0.18 (0.14)**	**0.26 (0.21)**

No statistical analysis provided for Serum Concentration of D-Dimer

3. Primary: Activated Protein C (APC) Resistance Ratio (Endogenous Thrombin Potential [ETP]-Based) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Activated Protein C (APC) Resistance Ratio (Endogenous Thrombin Potential [ETP]-Based)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). APC resistance ratio (ETP-based) measures the anticoagulation response of plasma to APC after activation of the extrinsic coagulation pathway. An increase in the ratio indicates a reduced responsiveness to APC. Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE

Number of Participants Analyzed [units: participants]	**60**	**58**
Activated Protein C (APC) Resistance Ratio (Endogenous Thrombin Potential [ETP]-Based) [units: Ratio] Mean (Standard Deviation)		
Baseline (n=59 NOMAC-E2; n=58 LNG-EE)	**0.80 (0.33)**	**0.83 (0.40)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**1.14 (0.45)**	**1.99 (0.76)**

Statistical Analysis 1 for Activated Protein C (APC) Resistance Ratio (Endogenous Thrombin Potential [ETP]-Based)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

4. Primary: Serum Concentration of Clotting Factor VIIa [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Clotting Factor VIIa
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo

	tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Clotting Factor VIIa [units: U/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**84 (32)**	**85 (37)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**118 (180)**	**98 (66)**

Statistical Analysis 1 for Serum Concentration of Clotting Factor VIIa

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.4191

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

5. Primary: Serum Concentration of Clotting Factor VIIc [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Clotting Factor VIIc
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or

another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Clotting Factor VIIc [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**105 (24)**	**105 (22)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**109 (31)**	**96 (25)**

Statistical Analysis 1 for Serum Concentration of Clotting Factor VIIc

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0010

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

6. Primary: Serum Concentration of Clotting Factor VIII [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Clotting Factor VIII
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum

	sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Clotting Factor VIII [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**93 (32)**	**95 (32)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**89 (34)**	**98 (30)**

Statistical Analysis 1 for Serum Concentration of Clotting Factor VIII

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.3779

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

7. Primary: Serum Concentration of Clotting Factor II [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Clotting Factor II
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Clotting Factor II [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**94 (11)**	**94 (12)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**95 (13)**	**97 (11)**

Statistical Analysis 1 for Serum Concentration of Clotting Factor II

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.5027

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:

	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

8. Primary: Serum Concentration of Antithrombin III [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Antithrombin III
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Antithrombin III [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**100 (10)**	**99 (11)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**102 (9)**	**96 (12)**

Statistical Analysis 1 for Serum Concentration of Antithrombin III

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel

P Value [3]	0.0041

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

9. Primary: Serum Concentration of Protein S (Free) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Protein S (Free)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Protein S (Free) [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**85 (16)**	**86 (14)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**99 (20)**	**99 (17)**

Statistical Analysis 1 for Serum Concentration of Protein S (Free)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.9662

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

10. Primary: Serum Concentration of Protein S (Total) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Protein S (Total)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**

Serum Concentration of Protein S (Total) [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	78 (12)	79 (10)
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	83 (12)	76 (9)

Statistical Analysis 1 for Serum Concentration of Protein S (Total)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0004

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

11. Primary: Serum Concentration of Protein C [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Protein C
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	60	58
Serum Concentration of Protein C [units: Percent of normal] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	107 (18)	103 (19)
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	108 (21)	113 (20)

Statistical Analysis 1 for Serum Concentration of Protein C

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0019

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

12. Primary: APC Resistance Ratio (Activated Partial Thromboplastin Time [APTT]-Based) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	APC Resistance Ratio (Activated Partial Thromboplastin Time [APTT]-Based)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). APC resistance ratio (APTT-based) measures the anticoagulation response of plasma to APC after activation of the intrinsic coagulation pathway. An increase in the ratio indicates a increased responsiveness to APC. Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
APC Resistance Ratio (Activated Partial Thromboplastin Time [APTT]-Based) [units: Ratio] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**1.01 (0.13)**	**1.00 (0.13)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**1.05 (0.13)**	**1.03 (0.12)**

Statistical Analysis 1 for APC Resistance Ratio (Activated Partial Thromboplastin Time [APTT]-Based)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.9662

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

13. Primary: Serum Concentration of Sex Hormone Binding Globulin (SHBG) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Sex Hormone Binding Globulin (SHBG)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.

Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Sex Hormone Binding Globulin (SHBG) [units: nmol/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**74 (34)**	**77 (26)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**108 (44)**	**100 (31)**

Statistical Analysis 1 for Serum Concentration of Sex Hormone Binding Globulin (SHBG)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0187

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

14. Primary: Serum Concentration of C-Reactive Protein (CRP) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of C-Reactive Protein (CRP)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of C-Reactive Protein (CRP) [units: mg/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**0.82 (1.16)**	**0.98 (1.35)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**1.32 (2.36)**	**4.43 (8.43)**

Statistical Analysis 1 for Serum Concentration of C-Reactive Protein (CRP)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:

	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

15. Primary: Serum Concentration of Total Cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Total Cholesterol
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Total Cholesterol [units: mmol/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**4.48 (0.87)**	**4.53 (0.82)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**4.51 (0.83)**	**4.48 (0.75)**

Statistical Analysis 1 for Serum Concentration of Total Cholesterol

Groups [1]	All groups

Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.6886

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

16. Primary: Serum Concentration of High Density Lipoprotein (HDL)-Cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of High Density Lipoprotein (HDL)-Cholesterol
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of High Density Lipoprotein (HDL)-Cholesterol [units: mmol/L] Mean (Standard Deviation)		

Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**1.63 (0.36)**	**1.68 (0.33)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**1.65 (0.34)**	**1.41 (0.26)**

Statistical Analysis 1 for Serum Concentration of High Density Lipoprotein (HDL)-Cholesterol

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

17. Primary: Serum Concentration of HDL2-cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of HDL2-cholesterol
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of HDL2-cholesterol [units: mmol/L] Mean (Standard Deviation)		
Baseline (n=58 NOMAC-E2; n=50 LNG-EE)	**0.63 (0.26)**	**0.69 (0.29)**
Cycle 6 (n=52 NOMAC-E2; n=51 LNG-EE)	**0.55 (0.25)**	**0.40 (0.18)**

Statistical Analysis 1 for Serum Concentration of HDL2-cholesterol

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

18. Primary: Serum Concentration of HDL3-cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of HDL3-cholesterol
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo

	tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of HDL3-cholesterol [units: mmol/L] Mean (Standard Deviation)		
Baseline (n=58 NOMAC-E2; n=50 LNG-EE)	**1.10 (0.16)**	**1.14 (0.19)**
Cycle 6 (n=52 NOMAC-E2; n=51 LNG-EE)	**1.16 (0.16)**	**1.10 (0.14)**

Statistical Analysis 1 for Serum Concentration of HDL3-cholesterol

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0083

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

19. Primary: Serum Concentration of Low Density Lipoprotein (LDL)-Cholesterol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Low Density Lipoprotein (LDL)-Cholesterol
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Low Density Lipoprotein (LDL)-Cholesterol [units: mmol/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**2.41 (0.73)**	**2.47 (0.66)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**2.40 (0.71)**	**2.61 (0.74)**

Statistical Analysis 1 for Serum Concentration of Low Density Lipoprotein (LDL)-Cholesterol

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0455

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

20. Primary: Serum Concentration of Apolipoprotein A-1 [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary

Measure Title	Serum Concentration of Apolipoprotein A-1
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Apolipoprotein A-1 [units: g/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**1.58 (0.27)**	**1.60 (0.25)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**1.78 (0.27)**	**1.67 (0.20)**

Statistical Analysis 1 for Serum Concentration of Apolipoprotein A-1

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0063

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No correction for multiple testing was made.

21. Primary: Serum Concentration of Apolipoprotein B [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Apolipoprotein B
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Apolipoprotein B [units: g/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**0.64 (0.17)**	**0.64 (0.15)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**0.68 (0.17)**	**0.80 (0.21)**

Statistical Analysis 1 for Serum Concentration of Apolipoprotein B

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:

	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

22. Primary: Serum Concentration of Lipoprotein(a) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Lipoprotein(a)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Lipoprotein(a) [units: g/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=57 LNG-EE)	**0.15 (0.18)**	**0.15 (0.14)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**0.17 (0.22)**	**0.12 (0.11)**

Statistical Analysis 1 for Serum Concentration of Lipoprotein(a)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

23. Primary: Serum Concentration of Total Triglycerides [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Total Triglycerides
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Total Triglycerides [units: mmol/L]		

Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	0.94 (0.30)	0.82 (0.23)
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	1.00 (0.37)	1.02 (0.32)

Statistical Analysis 1 for Serum Concentration of Total Triglycerides

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0078

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

24. Primary: Area Under the Curve Over 3 Hours (AUC3) for Glucose (Oral Glucose Tolerance Test [OGTT]) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Area Under the Curve Over 3 Hours (AUC3) for Glucose (Oral Glucose Tolerance Test [OGTT])
Measure Description	Blood glucose levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Area Under the Curve Over 3 Hours (AUC3) for Glucose (Oral Glucose Tolerance Test [OGTT]) [units: hrs*mmol/L] Mean (Standard Deviation)		
Baseline (n=59 NOMAC-E2; n=55 LNG-EE)	**15.82 (3.27)**	**14.44 (2.47)**
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	**16.09 (3.05)**	**16.69 (3.15)**

Statistical Analysis 1 for Area Under the Curve Over 3 Hours (AUC3) for Glucose (Oral Glucose Tolerance Test [OGTT])

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0016

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

25. Primary: Incremental AUC3 for Glucose (OGTT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Incremental AUC3 for Glucose (OGTT)
Measure Description	Blood glucose levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Incremental area under the curve was defined as incremental AUC3 = AUC3 - 3*fasting concentration. Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Incremental AUC3 for Glucose (OGTT) [units: hrs*mmol/L] Mean (Standard Deviation)		
Baseline (n=59 NOMAC-E2; n=55 LNG-EE)	**1.58 (3.05)**	**1.06 (2.55)**
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	**1.76 (2.72)**	**3.19 (3.03)**

Statistical Analysis 1 for Incremental AUC3 for Glucose (OGTT)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0003

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

26. Primary: AUC3 for Insulin (OGTT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	AUC3 for Insulin (OGTT)
Measure Description	Blood insulin levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)

Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
AUC3 for Insulin (OGTT) [units: hrs*pmol/L] Mean (Standard Deviation)		
Baseline (n=51 NOMAC-E2; n=50 LNG-EE)	**650 (298)**	**558 (182)**
Cycle 6 (n=46 NOMAC-E2; n=47 LNG-EE)	**658 (281)**	**721 (264)**

Statistical Analysis 1 for AUC3 for Insulin (OGTT)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0009

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

27. Primary: Incremental AUC3 for Insulin (OGTT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Incremental AUC3 for Insulin (OGTT)
Measure Description	Blood insulin levels were determined as fasting values just before oral glucose intake and each half hour thereafter for 2 hours and again after 3 hours. Oral glucose tolerance was analysed using the (unadjusted) area under the curve over the 3 hours (AUC3). Incremental area under the curve was defined as incremental AUC3 = AUC3 - 3*fasting concentration. Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Incremental AUC3 for Insulin (OGTT) [units: hrs*pmol/L] Mean (Standard Deviation)		
Baseline (n=51 NOMAC-E2; n=50 LNG-EE)	**517 (268)**	**451 (160)**
Cycle 6 (n=46 NOMAC-E2; n=47 LNG-EE)	**534 (239)**	**603 (237)**

Statistical Analysis 1 for Incremental AUC3 for Insulin (OGTT)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.0024

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:

	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

28. Primary: Serum Concentration of Hemoglobin Type A1c (HbA1c) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Hemoglobin Type A1c (HbA1c)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). HbA1c was determined before glucose loading. Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Hemoglobin Type A1c (HbA1c) [units: Percent of glycosylated hemoglobin] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**5.3 (0.3)**	**5.3 (0.2)**
Cycle 6 (n=53 NOMAC-E2; n=51 LNG-EE)	**5.3 (0.2)**	**5.4 (0.2)**

Statistical Analysis 1 for Serum Concentration of Hemoglobin Type A1c (HbA1c)

[1]	

Groups	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.3653

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

29. Primary: Serum Concentration of Total Cortisol [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Total Cortisol
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Total Cortisol [units: nmol/L] Mean (Standard Deviation)		

Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**482 (128)**	**502 (153)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**608 (167)**	**944 (183)**

Statistical Analysis 1 for Serum Concentration of Total Cortisol

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

30. Primary: Serum Concentration of Corticosteroid Binding Globulin (CBG) [Time Frame: Baseline to Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Corticosteroid Binding Globulin (CBG)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline to Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Corticosteroid Binding Globulin (CBG) [units: nmol/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**910 (201)**	**932 (163)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**1116 (252)**	**1980 (389)**

Statistical Analysis 1 for Serum Concentration of Corticosteroid Binding Globulin (CBG)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

31. Primary: Serum Concentration of Thyroid Stimulating Hormone (TSH) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Thyroid Stimulating Hormone (TSH)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description

NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Thyroid Stimulating Hormone (TSH) [units: mU/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**2.69 (1.28)**	**2.20 (1.08)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**2.96 (2.05)**	**2.75 (3.36)**

Statistical Analysis 1 for Serum Concentration of Thyroid Stimulating Hormone (TSH)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.5668

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

32. Primary: Serum Concentration of Free Thyroxine (T4) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Free Thyroxine (T4)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Free Thyroxine (T4) [units: pmol/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**14.0 (1.5)**	**14.1 (1.5)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**15.9 (2.0)**	**15.7 (2.1)**

Statistical Analysis 1 for Serum Concentration of Free Thyroxine (T4)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.1770

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

33. Primary: Serum Concentration of Thyroxin Binding Globulin (TBG) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Primary
Measure Title	Serum Concentration of Thyroxin Binding Globulin (TBG)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Thyroxin Binding Globulin (TBG) [units: mg/L] Mean (Standard Deviation)		
Baseline (n=60 NOMAC-E2; n=58 LNG-EE)	**20.3 (2.9)**	**20.3 (3.3)**
Cycle 6 (n=53 NOMAC-E2; n=52 LNG-EE)	**24.2 (3.6)**	**28.4 (5.3)**

Statistical Analysis 1 for Serum Concentration of Thyroxin Binding Globulin (TBG)

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	<.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	P-value compares the change from baseline to Cycle 6 between treatment groups.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel test adjusted for age class applied on the changes from baseline.

[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No correction for multiple testing was made.

34. Secondary: Serum Concentration of Total Testosterone [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Secondary
Measure Title	Serum Concentration of Total Testosterone
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Total Testosterone [units: nmol/L] Mean (Standard Deviation)		
Baseline (n=60, NOMAC-E2; n=58 LNG-EE)	**1.68 (0.75)**	**1.90 (0.94)**
Cycle 6 (n=53, NOMAC-E2; n=52 LNG-EE)	**1.23 (0.86)**	**0.91 (0.57)**

No statistical analysis provided for Serum Concentration of Total Testosterone

35. Secondary: Serum Concentration of Free Testosterone [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	

	Secondary
Measure Title	Serum Concentration of Free Testosterone
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Free Testosterone [units: pmol/L] Mean (Standard Deviation)		
Baseline (n=60, NOMAC-E2; n=58 LNG-EE)	**24.5 (14.9)**	**26.3 (16.6)**
Cycle 6 (n=53, NOMAC-E2; n=52 LNG-EE)	**12.8 (8.8)**	**9.9 (6.7)**

No statistical analysis provided for Serum Concentration of Free Testosterone

36. Secondary: Serum Concentration of Dehydroepiandrosterone Sulphate (DHEAS) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Secondary
Measure Title	Serum Concentration of Dehydroepiandrosterone Sulphate (DHEAS)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Dehydroepiandrosterone Sulphate (DHEAS) [units: umol/L] Mean (Standard Deviation)		
Baseline (n=60, NOMAC-E2; n=58 LNG-EE)	**4.94 (2.24)**	**5.19 (2.26)**
Cycle 6 (n=53, NOMAC-E2; n=52 LNG-EE)	**4.32 (1.82)**	**4.00 (1.91)**

No statistical analysis provided for Serum Concentration of Dehydroepiandrosterone Sulphate (DHEAS)

37. Secondary: Serum Concentration of Androstenedione [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Secondary
Measure Title	Serum Concentration of Androstenedione
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description

NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Androstenedione [units: nmol/L] Mean (Standard Deviation)		
Baseline (n=60, NOMAC-E2; n=58 LNG-EE)	**9.60 (3.45)**	**10.27 (3.91)**
Cycle 6 (n=53, NOMAC-E2; n=52 LNG-EE)	**8.23 (3.01)**	**6.96 (3.37)**

No statistical analysis provided for Serum Concentration of Androstenedione

38. Secondary: Serum Concentration of Dihydrotestosterone (DHT) [Time Frame: Baseline and Cycle 6 (between Days 15 and 21 of the cycle)]

Measure Type	Secondary
Measure Title	Serum Concentration of Dihydrotestosterone (DHT)
Measure Description	Serum samples were obtained under fasting conditions (no food or alcoholic beverages within 12 hours of serum sampling). Each cycle consists of 28 days.
Time Frame	Baseline and Cycle 6 (between Days 15 and 21 of the cycle)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All-participants-treated group; n = number of participants with non-missing baseline value and non-missing change from baseline to Cycle 6

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**60**	**58**
Serum Concentration of Dihydrotestosterone (DHT) [units: nmol/L] Mean (Standard Deviation)		
Baseline (n=60, NOMAC-E2; n=58 LNG-EE)	**0.59 (0.21)**	**0.62 (0.26)**
Cycle 6 (n=53, NOMAC-E2; n=52 LNG-EE)	**0.53 (0.28)**	**0.36 (0.19)**

No statistical analysis provided for Serum Concentration of Dihydrotestosterone (DHT)

39. Secondary: Number of In-treatment Pregnancies (With +2 Day Window) Per 100 Woman Years of Exposure (Pearl Index) [Time Frame: 6 cycles]

Measure Type	Secondary
Measure Title	Number of In-treatment Pregnancies (With +2 Day Window) Per 100 Woman Years of Exposure (Pearl Index)
Measure Description	In-treatment pregnancies were pregnancies with an estimated date of conception from the day of first intake of trial medication up to and including the day of last (active or placebo) intake of trial medication extended with a maximum of 2 days. Each 13 cycles (28 days per cycle) constitutes a woman year. The Pearl Index was obtained by dividing the number of in-treatment pregnancies that occurred by the time (in 100 women years) that the women were under risk of becoming pregnant.
Time Frame	6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The "restricted ITT" set included all participants treated and excluded nonpregnant participants who didn't have >=1 cycle expected to be at risk for pregnancy (with recorded use of condoms or w/o sexual intercourse per diary card data).

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**57**	**56**

Number of Woman years (rounded to nearest integer) Analyzed [units: Woman years (rounded to nearest integer)]	**23**	**22**
Number of In-treatment Pregnancies (With +2 Day Window) Per 100 Woman Years of Exposure (Pearl Index) [units: Pregnancies per 100 woman years] Number (95% Confidence Interval)	**0 (0 to 16.1)**	**0 (0 to 17.1)**

No statistical analysis provided for Number of In-treatment Pregnancies (With +2 Day Window) Per 100 Woman Years of Exposure (Pearl Index)

40. Secondary: Number of Participants With an Occurrence of Breakthrough Bleeding/Spotting [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Number of Participants With an Occurrence of Breakthrough Bleeding/Spotting
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough bleeding/spotting was defined as any episode that occurred during the "expected non-bleeding period" that was neither an early nor a continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT group consisted of all participants who were treated; ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length. n=number of participants with evaluable cycles.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**56**	**53**
Number of Participants With an Occurrence of Breakthrough Bleeding/Spotting [units: Participants]		

Cycle 1 (n=56 NOMAC-E2; n=53 LNG-EE)	**18**	**16**
Cycle 2 (n=55 NOMAC-E2; n=51 LNG-EE)	**11**	**9**
Cycle 3 (n=54 NOMAC-E2; n=52 LNG-EE)	**5**	**5**
Cycle 4 (n=54 NOMAC-E2; n=52 LNG-EE)	**8**	**2**
Cycle 5 (n=52 NOMAC-E2; n=51 LNG-EE)	**6**	**4**
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	**6**	**3**

No statistical analysis provided for Number of Participants With an Occurrence of Breakthrough Bleeding/Spotting

41. Secondary: Number of Participants With an Occurrence of Absence of Withdrawal Bleeding [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Number of Participants With an Occurrence of Absence of Withdrawal Bleeding
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Absence of withdrawal bleeding was defined as no bleeding/spotting episode that began during or continued into the "expected bleeding period". Expected bleeding period: NOMAC-E2: 7-day period starting on Day 25 of the cycle and ending on Day 3 of the next cycle; LNG-EE: 7-day period starting on Day 22 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT group consisted of all participants who were treated; ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length. n=number of participants with evaluable cycles.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**56**	**53**
Number of Participants With an Occurrence of Absence of Withdrawal Bleeding		

[units: Participants]		
Cycle 1 (n=56 NOMAC-E2; n=53 LNG-EE)	6	0
Cycle 2 (n=55 NOMAC-E2; n=51 LNG-EE)	8	1
Cycle 3 (n=54 NOMAC-E2; n=52 LNG-EE)	5	0
Cycle 4 (n=54 NOMAC-E2; n=52 LNG-EE)	8	0
Cycle 5 (n=52 NOMAC-E2; n=51 LNG-EE)	5	0
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	10	1

No statistical analysis provided for Number of Participants With an Occurrence of Absence of Withdrawal Bleeding

42. Secondary: Number of Participants With an Occurrence of Breakthrough Bleeding [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Number of Participants With an Occurrence of Breakthrough Bleeding
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough bleeding was defined as any bleeding episode that occurred during the "expected non-bleeding period" that was neither part of an early nor continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT group consisted of all participants who were treated; ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length. n=number of participants with evaluable cycles.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**
Number of Participants Analyzed [units: participants]	**56**	**53**

Number of Participants With an Occurrence of Breakthrough Bleeding [units: Participants]		
Cycle 1 (n=56 NOMAC-E2; n=53 LNG-EE)	3	1
Cycle 2 (n=55 NOMAC-E2; n=51 LNG-EE)	1	0
Cycle 3 (n=54 NOMAC-E2; n=52 LNG-EE)	1	0
Cycle 4 (n=54 NOMAC-E2; n=52 LNG-EE)	1	0
Cycle 5 (n=52 NOMAC-E2; n=51 LNG-EE)	2	0
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	3	0

No statistical analysis provided for Number of Participants With an Occurrence of Breakthrough Bleeding

43. Secondary: Number of Participants With an Occurrence of Breakthrough Spotting (Spotting Only) [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Number of Participants With an Occurrence of Breakthrough Spotting (Spotting Only)
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough spotting was defined as any spotting episode that occurred during the "expected non-bleeding period" that was neither part of an early nor continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT group consisted of all participants who were treated; ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length. n=number of participants with evaluable cycles.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**

Number of Participants Analyzed [units: participants]	**56**	**53**
Number of Participants With an Occurrence of Breakthrough Spotting (Spotting Only) [units: Participants]		
Cycle 1 (n=56 NOMAC-E2; n=53 LNG-EE)	**17**	**16**
Cycle 2 (n=55 NOMAC-E2; n=51 LNG-EE)	**10**	**9**
Cycle 3 (n=54 NOMAC-E2; n=52 LNG-EE)	**4**	**5**
Cycle 4 (n=54 NOMAC-E2; n=52 LNG-EE)	**7**	**2**
Cycle 5 (n=52 NOMAC-E2; n=51 LNG-EE)	**4**	**4**
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	**4**	**3**

No statistical analysis provided for Number of Participants With an Occurrence of Breakthrough Spotting (Spotting Only)

44. Secondary: Number of Participants With an Occurrence of Early Withdrawal Bleeding [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Number of Participants With an Occurrence of Early Withdrawal Bleeding
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Early withdrawal bleeding was defined as any withdrawal bleeding that started before the current "expected bleeding period". Expected bleeding period: NOMAC-E2: 7-day period starting on Day 25 of the cycle and ending on Day 3 of the next cycle; LNG-EE: 7-day period starting on Day 22 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT group consisted of all participants who were treated; ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length. n=number of participants with evaluable cycles.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	**LNG-EE**

Number of Participants Analyzed [units: participants]	**56**	**53**
Number of Participants With an Occurrence of Early Withdrawal Bleeding [units: Participants]		
Cycle 1 (n=56 NOMAC-E2; n=53 LNG-EE)	**5**	**4**
Cycle 2 (n=55 NOMAC-E2; n=51 LNG-EE)	**4**	**1**
Cycle 3 (n=54 NOMAC-E2; n=52 LNG-EE)	**3**	**1**
Cycle 4 (n=54 NOMAC-E2; n=52 LNG-EE)	**2**	**0**
Cycle 5 (n=52 NOMAC-E2; n=51 LNG-EE)	**1**	**0**
Cycle 6 (n=52 NOMAC-E2; n=50 LNG-EE)	**2**	**2**

No statistical analysis provided for Number of Participants With an Occurrence of Early Withdrawal Bleeding

45. Secondary: Number of Participants With an Occurrence of Continued Withdrawal Bleeding [Time Frame: Every 28-day cycle for 5 cycles]

Measure Type	Secondary
Measure Title	Number of Participants With an Occurrence of Continued Withdrawal Bleeding
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Continued withdrawal bleeding was defined as any withdrawal bleeding that continued into the "expected non-bleeding period" of the next cycle. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.
Time Frame	Every 28-day cycle for 5 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT group consisted of all participants who were treated; ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles. n= number of participants with evaluable cycles (except for the very last cycle of a participant for which this parameter was not defined).
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles. n= number of participants with evaluable cycles (except for the very last cycle of a participant for which this parameter was not defined).

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	56	53
Number of Participants With an Occurrence of Continued Withdrawal Bleeding [units: Participants]		
Cycle 1 (n=56 NOMAC-E2; n=53 LNG-EE)	15	25
Cycle 2 (n=54 NOMAC-E2; n=50 LNG-EE)	11	28
Cycle 3 (n=54 NOMAC-E2; n=52 LNG-EE)	13	26
Cycle 4 (n=53 NOMAC-E2; n=52 LNG-EE)	11	27
Cycle 5 (n=52 NOMAC-E2; n=51 LNG-EE)	13	29

No statistical analysis provided for Number of Participants With an Occurrence of Continued Withdrawal Bleeding

46. Secondary: Average Number of Breakthrough Bleeding/Spotting Days [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Average Number of Breakthrough Bleeding/Spotting Days
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Breakthrough bleeding/spotting was defined as any episode that occurred during the "expected non-bleeding period" that was neither an early nor a continued withdrawal bleeding. Expected non-bleeding period: NOMAC-E2: 21-day period starting on Day 4 of the cycle; LNG-EE: 21-day period starting on Day 1 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length. n=number of participants who had breakthrough bleeding/spotting for the respective cycle.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	56	53
Average Number of Breakthrough Bleeding/Spotting Days [units: Days] Mean (Standard Error)		
Cycle 1 (n=18 NOMAC-E2; n=16 LNG-EE)	3.5 (2.7)	4.6 (3.6)
Cycle 2 (n=11 NOMAC-E2; n=9 LNG-EE)	4.3 (1.4)	3.3 (2.2)
Cycle 3 (n=5 NOMAC-E2; n=5 LNG-EE)	4.6 (2.5)	3.2 (2.2)
Cycle 4 (n=8 NOMAC-E2; n=2 LNG-EE)	3.8 (2.3)	4.0 (0.0)
Cycle 5 (n=6 NOMAC-E2; n=4 LNG-EE)	3.3 (2.5)	2.0 (2.0)
Cycle 6 (n=6 NOMAC-E2; n=3 LNG-EE)	4.7 (3.7)	3.0 (2.0)

No statistical analysis provided for Average Number of Breakthrough Bleeding/Spotting Days

47. Secondary: Average Number of Withdrawal Bleeding/Spotting Days [Time Frame: Every 28-day cycle for 6 cycles]

Measure Type	Secondary
Measure Title	Average Number of Withdrawal Bleeding/Spotting Days
Measure Description	Cycle control was evaluated on the basis of vaginal bleeding pattern as recorded daily by participants using diary booklets. Participants documented whether vaginal bleeding was present, and if present, indicated whether it was considered to be spotting or bleeding. Withdrawal bleeding/spotting was defined as any episode that occurred during the "expected bleeding period". Expected bleeding period: NOMAC-E2: 7-day period starting on Day 25 of the cycle and ending on Day 3 of the next cycle; LNG-EE: 7-day period starting on Day 22 of the cycle.
Time Frame	Every 28-day cycle for 6 cycles
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

ITT analyses of vaginal bleeding patterns were based on all participants in the ITT group who had at least one evaluable cycle. Cycles were considered to be non-evaluable in case of insufficient bleeding data or improper cycle length.

n=number of participants who had withdrawal bleeding/spotting for the respective cycle.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo

	tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Measured Values

	NOMAC-E2	LNG-EE
Number of Participants Analyzed [units: participants]	**56**	**53**
Average Number of Withdrawal Bleeding/Spotting Days [units: Days] Mean (Standard Deviation)		
Cycle 1 (n=50 NOMAC-E2; n=53 LNG-EE)	**4.8 (2.3)**	**5.8 (3.6)**
Cycle 2 (n=47 NOMAC-E2; n=50 LNG-EE)	**4.7 (3.6)**	**4.9 (1.2)**
Cycle 3 (n=49 NOMAC-E2); n=52 LNG-EE)	**3.9 (2.0)**	**4.9 (1.4)**
Cycle 4 (n=46 NOMAC-E2; n=52 LNG-EE)	**4.0 (2.5)**	**5.0 (1.5)**
Cycle 5 (n=47 NOMAC-E2; n=51 LNG-EE)	**3.8 (1.7)**	**4.9 (1.5)**
Cycle 6 (n=42 NOMAC-E2; n=49 LNG-EE)	**3.5 (1.2)**	**4.2 (1.7)**

No statistical analysis provided for Average Number of Withdrawal Bleeding/Spotting Days

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Serious Adverse Events

	NOMAC-E2	LNG-EE
Total, serious adverse events		
# participants affected / at risk	**1/60 (1.67%)**	**0/58 (0.00%)**
Congenital, familial and genetic disorders		
Congenital mitral valve incompetence [1]		
# participants affected / at risk	**1/60 (1.67%)**	**0/58 (0.00%)**
# events	**1**	**0**

1 Term from vocabulary, MedDRA (10.1)

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
NOMAC-E2	Monophasic combined oral contraceptive (COC) tablets containing 2.5 mg Nomegestrol Acetate (NOMAC) and 1.5 mg Estradiol (E2) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-24, active tablets; Days 25-28, placebo tablets) for 6 consecutive 28-day cycles.
LNG-EE	Monophasic combined oral contraceptive (COC) tablets containing 0.150 mg levonorgestrel (LNG) and 0.030 mg ethinylestradiol (EE) taken once daily from Day 1 of menstrual period up to and including Day 28 (Days 1-21, active tablets; Days 22-28 placebo tablets) for 6 consecutive 28-day cycles.

Other Adverse Events

	NOMAC-E2	LNG-EE
Total, other (not including serious) adverse events		
# participants affected / at risk	**9/60 (15.00%)**	**18/58 (31.03%)**
Infections and infestations		
Influenza [1]		
# participants affected / at risk	**1/60 (1.67%)**	**4/58 (6.90%)**
# events	**1**	**4**
Upper respiratory tract infection [1]		
# participants affected / at risk	**6/60 (10.00%)**	**5/58 (8.62%)**

# events	**14**	**6**
Nervous system disorders		
Headache [1]		
# participants affected / at risk	**3/60 (5.00%)**	**7/58 (12.07%)**
# events	**5**	**14**
Skin and subcutaneous tissue disorders		
Acne [1]		
# participants affected / at risk	**2/60 (3.33%)**	**4/58 (6.90%)**
# events	**2**	**4**

1 Term from vocabulary, MedDRA (10.1)

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The SPONSOR recognizes the right of the investigator(s) to publish, but all publications must be based on data validated and released by the SPONSOR. Any such scientific paper, presentation, or other communication concerning the clinical trial will first be submitted to the SPONSOR, at least six weeks ahead of estimated publication or presentation, for consent, which shall not be withheld unreasonably.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
e-mail: ClinicalTrialsDisclosure@merck.com

Publications of Results:

Ågren UM, Anttila M, Mäenpää-Liukko K, Rantala ML, Rautiainen H, Sommer WF, Mommers E. Effects of a monophasic combined oral

contraceptive containing nomegestrol acetate and 17β-oestradiol compared with one containing levonorgestrel and ethinylestradiol on haemostasis, lipids and carbohydrate metabolism. Eur J Contracept Reprod Health Care. 2011 Dec;16(6):444-57. doi: 10.3109/13625187.2011.604450.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00511355 History of Changes
Other Study ID Numbers:	P05764 Organon Protocol No. 292004
Study First Received:	August 2, 2007
Results First Received:	July 28, 2011
Last Updated:	November 14, 2014
Health Authority:	Finland: Finnish Medicines Agency

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For Patients and Families | For Researchers | For Study Record Managers

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