ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: February 27, 2015

ClinicalTrials.gov ID: NCT01252186

Study Identification

Unique Protocol ID:	PSE-HSP-203
Brief Title:	A Multicenter Study to Evaluate the Effects of a 91-Day Extended Cycle Oral Contraceptive on Hemostatic Parameters in Healthy Women
Official Title:	A Multinational, Multicenter, Randomized, Open-Label Study to Evaluate the Impact of a 91-Day Extended Cycle Oral Contraceptive Regimen, Compared to Two 28-day Standard Oral Contraceptive Regimens, on Hemostatic Parameters in Healthy Women.
Secondary IDs:	2010-023215-34 [EudraCT Number]

Study Status

Record Verification:	February 2015
Overall Status:	Completed
Study Start:	November 2010 []
Primary Completion:	December 2011 [Actual]
Study Completion:	December 2011 [Actual]

Sponsor/Collaborators

Sponsor:	Teva Women's Health
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:

U.S. FDA-regulated Device:

Unapproved/Uncleared Device: No

U.S. FDA IND/IDE: Yes

IND/IDE Information: FDA Center: CDER
IND/IDE Number: 63735
Serial Number: 101
Has Expanded Access No

Human Subjects Review: Board Status: Approved
Approval Number: TEV1-10-355

[redacted]

Address:

[redacted]

Data Monitoring: No

FDA Regulated Intervention: Yes

Section 801 Clinical Trial: Yes

Study Description

Brief Summary: This study is being conducted to evaluate the impact of a 91-day extended cycle oral contraceptive compared to two 28-day oral contraceptive regimens on hemostatic parameters in healthy women.

Detailed Description:

Conditions

Conditions: Hemostasis
Oral Contraceptive

Keywords: Contraception

Hemostasis
Blood Coagulation

Study Design

Study Type:	Interventional
Primary Purpose:	Basic Science
Study Phase:	Phase 2
Interventional Study Model:	Parallel Assignment
Number of Arms:	3
Masking:	None (Open Label)
Allocation:	Randomized
Enrollment:	265 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 91-day Levonorgestrel Oral Contraceptive Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.	Drug: 91-day Levonorgestrel Oral Contraceptive 91-day treatment consisting of 84 blue combination tablets containing 150 µg LNG/30 µg EE and 7 yellow tablets containing 10 µg EE. Other Names: • Seasonique®
Active Comparator: 28-day Levonorgestrel Oral Contraceptive Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.	Drug: 28-day Levonorgestrel Oral Contraceptive 21 combination tablets containing 150 µg LNG/30 µg EE. Other Names: • Minidril®
Active Comparator: 28-day Desogestrel Oral Contraceptive Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.	Drug: 28-day Desogestrel Oral Contraceptive 21 combination tablets containing 150 µg DSG/30 µg EE. Other Names: • Marvelon®

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 40 Years

Sex: Female

Gender Based:

Accepts Healthy Volunteers: Yes

Criteria: Inclusion Criteria:

- Premenopausal, non-pregnant, non-lactating women age 18-40 years old
- Body Mass Index (BMI) ≥18 kg/m² and <30 kg/m²
- Regular spontaneous menstrual cycle
- Others as dictated by FDA-approved protocol

Exclusion Criteria:

- Any condition which contraindicates the use of combination oral contraceptives
- Any history of, or active, deep vein thrombosis, pulmonary embolism, or arterial thromboembolic disease within one year of screening
- Any known genetic component for thrombophilia including Factor V Leiden mutation, prothrombin mutation, protein C deficiency, protein S deficience, or antithrombin III deficiency
- Others as dictated by FDA-approved protocol

Contacts/Locations

Central Contact Person: Study Coordinator

[redacted]

Central Contact Backup: Study Coordinator

[redacted]

Study Officials: Teva Women's Health Research Protocol Chair
Study Chair
Teva Women's Health Research

Locations: United States, New Jersey
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United States, New York
Teva Investigational Site

Rochester, New York, United States, 14609

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Teva Investigational Site
Miami, Florida, United States, 33186

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Teva Investigational Site
San Antonio, Texas, United States, 78258

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San Diego, California, United States, 92108

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Teva Investigational Site
Seattle, Washington, United States, 98105

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Port Jefferson, New York, United States, 11777

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Houston, Texas, United States, 77054

United States, Pennsylvania
Teva Investigational Site
Pittsburgh, Pennsylvania, United States, 15206

United States, California
Teva Investigational Site
San Diego, California, United States, 92103

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Delayed Results

Delay Type	Certify Initial Approval
Intervention Name(s)	Levonorgestrel

Study Results

Participant Flow

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Overall Study

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Started	87	91	87

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Received Study Drug	83	89	80
Completed	57	59	53
Not Completed	30	32	34
Adverse Event	9	6	8
Withdrawal by Subject	2	5	2
Physician Decision	0	0	1
Non-compliance	0	3	4
Protocol Violation	0	0	1
Pregnancy	2	2	0
Sponsor Request	2	1	0
Lost to Follow-up	10	10	11
Other - Miscellaneous Reasons	5	5	7

Baseline Characteristics

Baseline Analysis Population Description

The intent-to-treat (ITT) population included all randomized and treated participants who had both baseline and at least one post-baseline measurement of prothrombin fragment 1+2 (F1+2).

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.

	Description
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Baseline Measures

		91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive	Total
Overall Number of Participants		75	80	71	226
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	75 participants	80 participants	71 participants	226 participants
		27.3 (5.87)	26.8 (6.22)	27.0 (5.75)	27.0 (5.94)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	75 participants	80 participants	71 participants	226 participants
	Female	75 100%	80 100%	71 100%	226 100%
	Male	0 0%	0 0%	0 0%	0 0%
Race/Ethnicity, Customized Measure Type: Number Unit of measure: participants	Number Analyzed	75 participants	80 participants	71 participants	226 participants
Asian		1	5	3	9
Black or African-American		18	15	9	42
Caucasian		42	39	40	121
Hispanic		13	20	19	52
Other		1	1	0	2

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Prothrombin Fragment 1+2 Levels
Measure Description	Prothrombin fragment 1+2 is a coagulation factor, released when prothrombin is cleaved by activated factor X. Elevated plasma levels of prothrombin fragment 1+2 indicate high risk of thrombosis.
Time Frame	Baseline to Month 6

Analysis Population Description

Per-Protocol (PP) Population included all data from ITT participants obtained prior to experiencing major protocol violations.

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Prothrombin Fragment 1+2 Levels Least Squares Mean (Standard Error) Unit of measure: pmol/L	169.53 (155.15)	157.99 (150.11)	592.29 (160.32)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Prothrombin Fragment 1+2 Levels

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The primary endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.

	Type of Statistical Test	Non-Inferiority or Equivalence (legacy)
	Comments	A conclusion of non-inferiority was reached if the lower limit of the confidence interval for the comparison (active control minus 91-day Levonorgestrel) was greater than -0.13 nmol/L (130 pmol/L).

Statistical Test of Hypothesis	P-Value	0.958
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-11.54
	Confidence Interval	(2-Sided) 95% -440.1 to 417.0
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel – 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Prothrombin Fragment 1+2 Levels

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The primary endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Non-Inferiority or Equivalence (legacy)
	Comments	A conclusion of non-inferiority was reached if the lower limit of the confidence interval for the comparison (active control minus 91-day Levonorgestrel) was greater than -0.13 nmol/L (130 pmol/L).

Statistical Test of Hypothesis	P-Value	0.060
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	422.76
	Confidence Interval	(2-Sided) 95% -18.3 to 863.8

	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel – 91-day Levonorgestrel)

2. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in D-dimer
Measure Description	D-dimer is the degradation product of cross-linked fibrin and is a marker of thrombin and fibrin formation and turnover.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in D-dimer Least Squares Mean (Standard Error) Unit of measure: ng/mL	86.74 (31.49)	72.43 (30.18)	158.05 (32.07)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in D-dimer

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.745
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-14.31
	Confidence Interval	(2-Sided) 95% -100.8 to 72.2
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in D-dimer

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.115
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	71.31
	Confidence Interval	(2-Sided) 95% -17.5 to 160.1
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Plasmin-Antiplasmin (PAP) Complex

Measure Description	The plasmin-antiplasmin (PAP) complex is a marker of thrombin and fibrin formation and turnover.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Plasmin-Antiplasmin (PAP) Complex Least Squares Mean (Standard Error) Unit of measure: ng/mL	10.72 (44.55)	-6.42 (43.11)	107.81 (45.97)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Plasmin-Antiplasmin (PAP) Complex

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.782
	Comments	[Not specified]

	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-17.14
	Confidence Interval	(2-Sided) 95% -139.4 to 105.1
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Plasmin-Antiplasmin (PAP) Complex

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.131
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	97.09
	Confidence Interval	(2-Sided) 95% -29.2 to 223.4
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Activated Partial Thromboplastin Time (APTT) Based Activated Protein-C Resistance (APC)

Measure Description	The APC resistance assay is a clotting test that measures the ratio of APTT clotting times in the presence and absence of a standard amount of exogenous APC. APC resistance is calculated as the ratio of the clotting time after APC addition over the clotting time with no APC addition. APC resistance is defined as a poor anticoagulant response of plasma to APC (minimal prolongation of the APTT) and a correspondingly low ratio.
Time Frame	Baseline to Month 6

Analysis Population Description

Per-protocol population with available data

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	58
Change From Baseline to End of Month 6 in Activated Partial Thromboplastin Time (APTT) Based Activated Protein-C Resistance (APC) Least Squares Mean (Standard Error) Unit of measure: ratio	-0.12 (0.04)	-0.15 (0.03)	-0.27 (0.04)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Activated Partial Thromboplastin Time (APTT) Based Activated Protein-C Resistance (APC)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.

	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.428
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.04
	Confidence Interval	(2-Sided) 95% -0.1 to 0.1
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Activated Partial Thromboplastin Time (APTT) Based Activated Protein-C Resistance (APC)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.16
	Confidence Interval	(2-Sided) 95% -0.3 to -0.1
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Endogenous Thrombin Potential (EPT) Based Activated Protein-C Resistance (APC)
Measure Description	This assay is based on measurement of the effect of activated protein C on the endogenous thrombin potential, the time integral of thrombin generation initiated in plasma through the extrinsic coagulation pathway. The APC resistance assay measures the ratio of endogenous thrombin potential in the presence and absence of a standard amount of exogenous APC. APC resistance is calculated as the ratio of EPT after APC addition over the EPT with no APC addition. APC resistance is defined as a poor anticoagulant response of plasma to APC (less inhibition of thrombin formation) and a correspondingly higher ratio.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Endogenous Thrombin Potential (EPT) Based Activated Protein-C Resistance (APC) Least Squares Mean (Standard Error) Unit of measure: ratio	0.38 (0.05)	0.37 (0.05)	0.57 (0.05)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Endogenous Thrombin Potential (EPT) Based Activated Protein-C Resistance (APC)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.868
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.01
	Confidence Interval	(2-Sided) 95% -0.2 to 0.1
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Endogenous Thrombin Potential (EPT) Based Activated Protein-C Resistance (APC)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.012
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	0.20
	Confidence Interval	(2-Sided) 95%

		0.0 to 0.3
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Fibrinogen
Measure Description	Fibrinogen (factor I) is a glycoprotein that helps in the formation of blood clots.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Fibrinogen Least Squares Mean (Standard Error) Unit of measure: g/L	0.12 (0.07)	0.22 (0.06)	-0.04 (0.07)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Fibrinogen

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive

	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.317
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	0.09
	Confidence Interval	(2-Sided) 95% -0.1 to 0.3
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Fibrinogen

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.081
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.16
	Confidence Interval	(2-Sided) 95% -0.4 to 0.0

	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

7. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Plasminogen
Measure Description	Plasminogen is the precursor of plasmin, which lyses fibrin clots.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Plasminogen Least Squares Mean (Standard Error) Unit of measure: g/L	0.04 (0.00)	0.04 (0.00)	0.04 (0.00)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Plasminogen

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.

	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.331
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.004
	Confidence Interval	(2-Sided) 95% -0.013 to 0.004
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Plasminogen

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.173
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.006
	Confidence Interval	(2-Sided) 95% -0.015 to 0.003
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

8. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Tissue Plasminogen Activator (t-PA)
Measure Description	Tissue plasminogen activator catalyzes the conversion of plasminogen to plasmin, the major enzyme responsible for the breakdown of blood clots.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Tissue Plasminogen Activator (t-PA) Least Squares Mean (Standard Error) Unit of measure: µg/L	-0.91 (0.32)	-1.48 (0.30)	-9.3 (0.32)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Tissue Plasminogen Activator (t-PA)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.194
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.57
	Confidence Interval	(2-Sided) 95% -1.4 to 0.3
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Tissue Plasminogen Activator (t-PA)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.967
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.02
	Confidence Interval	(2-Sided) 95% -0.9 to 0.9
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

9. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Factor II

Measure Description	Clotting factor II, also called prothrombin, functions in blood coagulation. Results are reported as percent of normal plasma concentrations. By definition, normal plasma contains 100% (1 unit/mL) of each factor. The reference range is approximately 60% to 140% for adults.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Factor II Least Squares Mean (Standard Error) Unit of measure: percentage of normal	6.89 (1.73)	7.98 (1.65)	8.57 (1.76)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Factor II

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.648
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	1.09
	Confidence Interval	(2-Sided) 95% -3.6 to 5.8
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Factor II

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.496
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	1.68
	Confidence Interval	(2-Sided) 95% -3.2 to 6.6
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

10. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Factor VII

Measure Description	Clotting factor VII, also called proconvertin or autoprothrombin I, functions in blood coagulation. Results are reported as percent of normal plasma concentrations. By definition, normal plasma contains 100% (1 unit/mL) of each factor. The reference range is approximately 60% to 140% for adults.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Factor VII Least Squares Mean (Standard Error) Unit of measure: percentage of normal	14.27 (7.52)	22.98 (7.18)	43.22 (7.67)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Factor VII

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.405
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	8.71
	Confidence Interval	(2-Sided) 95% -11.9 to 29.3
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Factor VII

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.008
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	28.95
	Confidence Interval	(2-Sided) 95% 7.7 to 50.2
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

11. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Factor VIII

Measure Description	Clotting factor VIII, also known as anti-hemophilic factor (AHF), functions in blood coagulation by stabilizing fibrin clots. Results are reported as a percent of the amount expected in normal plasma. By definition, the mean value in normal plasma is 100%. The reference range is approximately 70% to 140%.for adults.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Factor VIII Least Squares Mean (Standard Error) Unit of measure: percentage of normal	-3.23 (2.98)	0.08 (2.87)	5.53 (3.05)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Factor VIII

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.425
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	3.30
	Confidence Interval	(2-Sided) 195% -4.9 to 11.5
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Factor VIII

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.041
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	8.76
	Confidence Interval	(2-Sided) 95% 0.3 to 17.2
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

12. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Antithrombin

Measure Description	Antithrombin is a protein in the blood that naturally blocks blood clots from forming. Results are reported as a percent of the amount expected in normal plasma. By definition, the mean value in normal plasma is 100%. The reference range is approximately 80% to 130%.for adults.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Antithrombin Least Squares Mean (Standard Error) Unit of measure: percentage of normal	2.36 (1.00)	-0.05 (0.98)	-0.83 (1.03)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Antithrombin

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.088
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-2.40
	Confidence Interval	(2-Sided) 95% -5.2 to 0.4
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Antithrombin

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.028
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-3.19
	Confidence Interval	(2-Sided) 95% -6.0 to -0.3
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

13. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Protein C Activity

Measure Description	Protein C helps to regulate blood clot formation. Activated Protein C (APC) combines with Protein S (a cofactor) to degrade coagulation factors VIIIa and Va, slowing down the generation of new thrombin and inhibiting further clotting. Results are reported as a percent of the amount expected in normal plasma. By definition, the mean value in normal plasma is 100%. The reference range is approximately 70% to 140% for adults.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Protein C Activity Least Squares Mean (Standard Error) Unit of measure: percentage of normal	-6.15 (2.62)	-4.39 (2.53)	-2.41 (2.70)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Protein C Activity

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.631
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	1.75
	Confidence Interval	(2-Sided) 95% -5.4 to 8.9
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Protein C Activity

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.323
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	3.73
	Confidence Interval	(2-Sided) 95% -3.7 to 11.2
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

14. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Protein C Antigen

Measure Description	Protein C helps to regulate blood clot formation. Activated Protein C (APC) combines with Protein S (a cofactor) to degrade coagulation factors VIIIa and Va, slowing down the generation of new thrombin and inhibiting further clotting. Results are reported as a percent of the amount expected in normal plasma. By definition, the mean value in normal plasma is 100%. The reference range is approximately 70% to 140% in adults.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Protein C Antigen Least Squares Mean (Standard Error) Unit of measure: percentage of normal	12.83 (2.26)	11.97 (2.17)	10.00 (2.32)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Protein C Antigen

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.783
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.86
	Confidence Interval	(2-Sided) 595% -7.0 to 5.3
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Protein C Antigen

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.384
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-2.83
	Confidence Interval	(2-Sided) 95% -9.2 to 3.6
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

15. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Free Protein S

Measure Description	Protein S helps to regulate blood clot formation. Protein S exists in two forms: a free form and a complex form. Free protein S combines with Protein C to degrade coagulation factors VIIIa and Va, slowing down the generation of new thrombin and inhibiting further clotting. Results are reported as a percent of the amount expected in normal plasma. By definition, the mean value in normal plasma is 100%. The reference range is approximately 70% to 140%; lower for women than for men.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Free Protein S Least Squares Mean (Standard Error) Unit of measure: percentage of normal	2.96 (2.13)	4.62 (2.03)	-18.2 (2.17)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Free Protein S

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.572
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	1.66
	Confidence Interval	(2-Sided) 95% -4.1 to 7.5
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Free Protein S

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-20.98
	Confidence Interval	(2-Sided) 95% -27.0 to -15.0
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

16. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Total Protein S

Measure Description	Protein S helps to regulate blood clot formation. Protein S exists in two forms: a free form and a complex form. Free protein S combines with activated protein C to degrade coagulation factors VIIIa and Va, slowing down the generation of new thrombin and inhibiting further clotting. Results are reported as a percent of the amount expected in normal plasma. By definition, the mean value in normal plasma is 100%. The reference range is approximately 70% to 140%; lower for women than for men.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Total Protein S Least Squares Mean (Standard Error) Unit of measure: percentage of normal	-11.06 (1.51)	-11.48 (1.45)	-21.59 (1.55)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Total Protein S

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.841
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-0.42
	Confidence Interval	(2-Sided) 95% -4.6 to 3.7
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Total Protein S

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-10.53
	Confidence Interval	(2-Sided) 95% -14.8 to -6.3
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

17. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Tissue Factor Pathway Inhibitor (TFPI)

Measure Description	Tissue Factor Pathway Inhibitor (TFPI) is an anti-coagulation protein that binds to activated protein X.
Time Frame	Baseline to Month 6

Analysis Population Description
Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Tissue Factor Pathway Inhibitor (TFPI) Least Squares Mean (Standard Error) Unit of measure: ng/mL	4.65 (1.26)	2.54 (1.21)	-1.34 (1.30)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Tissue Factor Pathway Inhibitor (TFPI)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.227
	Comments	[Not specified]

	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-2.11
	Confidence Interval	(2-Sided) 95% -5.6 to 1.3
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Tissue Factor Pathway Inhibitor (TFPI)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.001
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-5.99
	Confidence Interval	(2-Sided) 95% -9.6 to -2.4
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

18. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Thyroid Stimulating Hormone (TSH)
Measure Description	
Time Frame	Baseline top Month 6

Analysis Population Description

Per-protocol population with available data

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	58
Change From Baseline to End of Month 6 in Thyroid Stimulating Hormone (TSH) Least Squares Mean (Standard Error) Unit of measure: mIU/L	-0.22 (0.13)	0.10 (0.13)	0.22 (0.13)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Thyroid Stimulating Hormone (TSH)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.076
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	0.33
	Confidence Interval	(2-Sided) 95% -0.0 to 0.7
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Thyroid Stimulating Hormone (TSH)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.021
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	0.44
	Confidence Interval	(2-Sided) 95% 0.1 to 0.8
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

19. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Total Cortisol
Measure Description	
Time Frame	Baseline to Month 6

Analysis Population Description

Per-protocol population

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	59
Change From Baseline to End of Month 6 in Total Cortisol Least Squares Mean (Standard Error) Unit of measure: nmol/L	217.94 (24.39)	262.40 (23.39)	227.68 (24.96)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Total Cortisol

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.190
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	44.46

	Confidence Interval	(2-Sided) 95% -22.3 to 111.2
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Total Cortisol

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.781
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	9.74
	Confidence Interval	(2-Sided) 95% -59.4 to 78.9
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

20. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Corticosteroid Binding Globulin
Measure Description	
Time Frame	Baseline to Month 6

Analysis Population Description

Per-protocol population with available data

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	67	58
Change From Baseline to End of Month 6 in Corticosteroid Binding Globulin Least Squares Mean (Standard Error) Unit of measure: nmol/L	576.33 (45.37)	563.85 (43.41)	634.64 (46.74)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Corticosteroid Binding Globulin

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.843
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-12.49

	Confidence Interval	(2-Sided) 95% -136.4 to 111.4
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Corticosteroid Binding Globulin

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.376
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	58.30
	Confidence Interval	(2-Sided) 95% -71.3 to 187.9
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

21. Secondary Outcome Measure:

Measure Title	Change From Baseline to End of Month 6 in Sex Hormone Binding Globulin (SHBG)
Measure Description	
Time Frame	Baseline to Month 6

Analysis Population Description

Per-protocol population with available data

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

Measured Values

	91-day Levonorgestrel Oral Contraceptive	28-day Levonorgestrel Oral Contraceptive	28-day Desogestrel Oral Contraceptive
Overall Number of Participants Analyzed	61	66	58
Change From Baseline to End of Month 6 in Sex Hormone Binding Globulin (SHBG) Least Squares Mean (Standard Error) Unit of measure: mIU/L	34.87 (8.40)	30.85 (8.08)	165.01 (8.67)

Statistical Analysis 1 for Change From Baseline to End of Month 6 in Sex Hormone Binding Globulin (SHBG)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Levonorgestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.731
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	-4.01

	Confidence Interval	(2-Sided) 95% -27.0 to 19.0
	Estimation Comments	Treatment difference is calculated as (28-day Levonorgestrel - 91-day Levonorgestrel)

Statistical Analysis 2 for Change From Baseline to End of Month 6 in Sex Hormone Binding Globulin (SHBG)

Statistical Analysis Overview	Comparison Group Selection	91-day Levonorgestrel Oral Contraceptive, 28-day Desogestrel Oral Contraceptive
	Comments	The endpoint was analyzed using a maximum likelihood-based mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) with covariate adjustment for baseline, treatment, month, and the treatment-by-month interaction.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Treatment Difference]
	Estimated Value	130.15
	Confidence Interval	(2-Sided) 95% 106.2 to 154.1
	Estimation Comments	Treatment difference is calculated as (28-day Desogestrel - 91-day Levonorgestrel)

Reported Adverse Events

Time Frame	From the first dose of study drug until 14 days after the last dose (up to 27 weeks).
Adverse Event Reporting Description	[Not specified]

Reporting Groups

	Description
91-day Levonorgestrel Oral Contraceptive	Participants received 12 weeks (84 consecutive days) of active combination tablets containing 150 µg levonorgestrel (LNG)/30 µg ethinyl estradiol (EE), followed by 7 days of 10 µg EE monotherapy in each 91-day cycle for a total of two 91-day cycles.

	Description
28-day Levonorgestrel Oral Contraceptive	Participants received 21 days of active combination tablets containing 150 µg LNG/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.
28-day Desogestrel Oral Contraceptive	Participants received 21 days of active combination tablets (containing 150 µg desogestrel (DSG)/30 µg EE, followed by no treatment for 7 days in each 28-day cycle for a total of six 28-day cycles.

All-Cause Mortality

	91-day Levonorgestrel Oral Contraceptive		28-day Levonorgestrel Oral Contraceptive		28-day Desogestrel Oral Contraceptive	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total All-Cause Mortality	/		/		/	

Serious Adverse Events

	91-day Levonorgestrel Oral Contraceptive		28-day Levonorgestrel Oral Contraceptive		28-day Desogestrel Oral Contraceptive	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	0/83 (0%)		0/89 (0%)		0/80 (0%)	

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	91-day Levonorgestrel Oral Contraceptive		28-day Levonorgestrel Oral Contraceptive		28-day Desogestrel Oral Contraceptive	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	16/83 (19.28%)		10/89 (11.24%)		17/80 (21.25%)	
Gastrointestinal disorders						
Nausea [A] *	5/83 (6.02%)	5	4/89 (4.49%)	5	8/80 (10%)	9
Infections and infestations						
Urinary tract infection [A] *	0/83 (0%)	0	2/89 (2.25%)	2	4/80 (5%)	4
Investigations						
Prothrombin level increased [A] *	0/83 (0%)	0	1/89 (1.12%)	1	4/80 (5%)	4

	91-day Levonorgestrel Oral Contraceptive		28-day Levonorgestrel Oral Contraceptive		28-day Desogestrel Oral Contraceptive	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Nervous system disorders						
Headache [A] *	3/83 (3.61%)	3	1/89 (1.12%)	1	4/80 (5%)	4
Reproductive system and breast disorders						
Metrorrhagia [A] *	11/83 (13.25%)	14	3/89 (3.37%)	3	2/80 (2.5%)	2

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA V9.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

Sponsor has the right 60 days before submission for publication to review/provide comments. If the Sponsor’s review shows that potentially patentable subject matter would be disclosed, publication or public disclosure shall be delayed for up to 90 additional days in order for the Sponsor, or Sponsor’s designees, to file the necessary patent applications. In multicenter trials, each PI will postpone single center publications until after disclosure or publication of multicenter data.

Results Point of Contact:

Name/Official Title: Director, Clinical Research
Organization: Teva Branded Pharmaceutical Products, R&D Inc.