



## Clinical trial results:

### A Double-Blind, Randomised, Placebo Controlled, Adaptive Design Study of the Efficacy, Safety and Pharmacokinetics of NT-814 in Female Subjects With Moderate to Severe Vasomotor Symptoms Associated With the Menopause

#### Summary

EudraCT number	2018-002763-26
Trial protocol	GB
Global end of trial date	21 November 2019

#### Results information

Result version number	v1
This version publication date	05 December 2020
First version publication date	05 December 2020

#### Trial information

##### Trial identification

Sponsor protocol code	BAY3427080/21686
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03596762
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 November 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Primary Objectives:

- To evaluate the efficacy of once daily doses of 40 mg, 80 mg, 120 mg and 160 mg BAY3427080 (NT-814), compared with placebo, in reducing the frequency and severity of hot flashes.
- To assess the safety and tolerability of once daily doses of 40 mg, 80 mg, 120 mg and 160 mg BAY3427080 (NT-814), compared with placebo, in subjects with post-menopausal symptoms.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Only after the subject voluntarily signed the informed consent form was he/she able to enter the study. If the subject was not capable of providing a signature, an oral statement of consent could have been given in the presence of a witness. Each subject was assured of the right to withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	United Kingdom: 95
Country: Number of subjects enrolled	United States: 71
Worldwide total number of subjects	199
EEA total number of subjects	95

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	198
From 65 to 84 years	1
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted between 20 November 2018 (first subject, first visit) and 21 November 2019 (last subject, last visit) at 11 sites in the USA, nine sites in the UK, and five sites in Canada.

### Pre-assignment

Screening details:

A total of 760 subjects were screened, of whom 199 completed screening and were randomised. Not meeting the eligibility criteria was the reason provided for all screening failures (561). A total of 47 subjects were randomised to placebo and 152 subjects to BAY3427080 (NT-814).

### Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo

Arm description:

Subjects received four placebo capsules orally once daily in the evening before bedtime.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

4 x placebo capsules

<b>Arm title</b>	40 mg BAY3427080
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Arm description:

Subjects received one 40 mg BAY3427080 capsule and 3 placebo capsules.

Arm type	Experimental
Investigational medicinal product name	BAY3427080
Investigational medicinal product code	
Other name	NT-814
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

one capsule of 40 mg BAY3427080 once daily in the evening before bedtime.

<b>Arm title</b>	80 mg BAY3427080
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Arm description:

subjects received 2x40 mg BAY3427080 capsules and 2 placebo capsules.

Arm type	Experimental
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Investigational medicinal product name	BAY3427080
Investigational medicinal product code	
Other name	NT-814
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Two capsules of 40 mg BAY3427080 once daily in the evening before bedtime.

<b>Arm title</b>	120 mg BAY3427080
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Arm description:

Subjects received 3x40 mg BAY3427080 capsules and 1 placebo capsule.

Arm type	Experimental
Investigational medicinal product name	BAY3427080
Investigational medicinal product code	
Other name	NT-814
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Three capsules of 40 mg BAY3427080 once daily in the evening before bedtime.

<b>Arm title</b>	160 mg BAY3427080
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Arm description:

Subjects received 4x40 mg BAY3427080 capsules.

Arm type	Experimental
Investigational medicinal product name	BAY3427080
Investigational medicinal product code	
Other name	NT-814
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Four capsules of 40 mg BAY3427080 once daily in the evening before bedtime.

<b>Number of subjects in period 1</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080
Started	47	31	17
Completed	43	30	16
Not completed	4	1	1
Consent withdrawn by subject	2	1	-
Adverse event, non-fatal	2	-	1
Protocol deviation	-	-	-

<b>Number of subjects in period 1</b>	120 mg BAY3427080	160 mg BAY3427080
Started	52	52
Completed	51	45
Not completed	1	7
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	5
Protocol deviation	-	1



## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received four placebo capsules orally once daily in the evening before bedtime.	
Reporting group title	40 mg BAY3427080
Reporting group description: Subjects received one 40 mg BAY3427080 capsule and 3 placebo capsules.	
Reporting group title	80 mg BAY3427080
Reporting group description: subjects received 2x40 mg BAY3427080 capsules and 2 placebo capsules.	
Reporting group title	120 mg BAY3427080
Reporting group description: Subjects received 3x40 mg BAY3427080 capsules and 1 placebo capsule.	
Reporting group title	160 mg BAY3427080
Reporting group description: Subjects received 4x40 mg BAY3427080 capsules.	

Reporting group values	Placebo	40 mg BAY3427080	80 mg BAY3427080
Number of subjects	47	31	17
Age Categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	55.6	55.4	55.9
standard deviation	± 4.1	± 4.0	± 4.2
Gender Categorical Units: Subjects			
Female	47	31	17
Male	0	0	0
Race Units: Subjects			
Asian	2	0	0
Black or African American	6	5	3
White	38	24	13
Other	1	2	1
Ethnicity			

Units: Subjects			
Hispanic or Latino	2	2	1
Not Hispanic or Latino	45	29	16

  

<b>Reporting group values</b>	120 mg BAY3427080	160 mg BAY3427080	Total
Number of subjects	52	52	199
Age Categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	54.8	55.0	-
standard deviation	± 4.4	± 3.8	
Gender Categorical Units: Subjects			
Female	52	52	199
Male	0	0	0
Race Units: Subjects			
Asian	1	1	4
Black or African American	13	11	38
White	37	40	152
Other	1	0	5
Ethnicity Units: Subjects			
Hispanic or Latino	2	6	13
Not Hispanic or Latino	50	46	186



## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received four placebo capsules orally once daily in the evening before bedtime.	
Reporting group title	40 mg BAY3427080
Reporting group description: Subjects received one 40 mg BAY3427080 capsule and 3 placebo capsules.	
Reporting group title	80 mg BAY3427080
Reporting group description: subjects received 2x40 mg BAY3427080 capsules and 2 placebo capsules.	
Reporting group title	120 mg BAY3427080
Reporting group description: Subjects received 3x40 mg BAY3427080 capsules and 1 placebo capsule.	
Reporting group title	160 mg BAY3427080
Reporting group description: Subjects received 4x40 mg BAY3427080 capsules.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects who received at least one dose of double-blind study drug, irrespective of treatment received. Subjects were analysed according to treatment received.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: All randomised subjects who received at least one dose of double-blind study drug, irrespective of treatment received, and had hot flush data for at least 7 days' worth of post-treatment assessments (i.e. requirement for primary efficacy endpoint). Subjects were analysed according to randomised treatment.	
Subject analysis set title	Per Protocol (PP) Set
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the FAS who completed the 12-week treatment period excluding those identified as having relevant protocol deviations.	

### Primary: Mean change from baseline in mean daily frequency of moderate and severe hot flushes from baseline to Week 4

End point title	Mean change from baseline in mean daily frequency of moderate and severe hot flushes from baseline to Week 4
End point description: Subjects recorded daily in their electronic diary (eDiary) the frequency and severity of hot flushes during the treatment period. The baseline assessment for hot flushes was calculated using the last 7 days (not necessarily consecutive days) with an available data in the evening and/or the morning of the baseline diary completion period. A diary day was comprised of the evening entry of this day and the morning entry of the following day, in that order. Mean daily frequency = Sum of number of hot flushes filled in the diary during the last 7 diary days (with at least one available data in the evening and/or morning) divided by 7. Moderate: Sensation of heat with sweating, but able to continue activity. Severe: Sensation of heat with sweating, causing cessation (stopping) of activity. In categories the number of subjects analyzed (N) at week 4 is mentioned for each reporting group respectively.	
End point type	Primary
End point timeframe: From baseline to week 4	

<b>End point values</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	11.82 (± 4.42)	12.13 (± 8.81)	14.55 (± 5.87)	13.54 (± 7.17)
Week 4: Change from baseline (N=45,31,17,52,47)	-2.45 (± 3.65)	-4.19 (± 5.78)	-4.30 (± 6.45)	-6.76 (± 5.85)

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	12.92 (± 6.90)			
Week 4: Change from baseline (N=45,31,17,52,47)	-5.42 (± 5.36)			

## Statistical analyses

<b>Statistical analysis title</b>	40 mg BAY3427080 versus placebo
Comparison groups	Placebo v 40 mg BAY3427080
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1946
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.83
upper limit	0.78

<b>Statistical analysis title</b>	80 mg BAY3427080 versus placebo
Comparison groups	Placebo v 80 mg BAY3427080

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3682
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.11
upper limit	1.53

<b>Statistical analysis title</b>	120 mg BAY3427080 versus placebo
Comparison groups	Placebo v 120 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-3.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.94
upper limit	-1.92

<b>Statistical analysis title</b>	160 mg BAY3427080 versus placebo
Comparison groups	Placebo v 160 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0115
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-2.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.66
upper limit	-0.6

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### Primary: Mean change from baseline in mean daily frequency of moderate and

**severe hot flushes from baseline to Week 12**

End point title	Mean change from baseline in mean daily frequency of moderate and severe hot flushes from baseline to Week 12
End point description: Subjects recorded daily in their electronic diary (eDiary) the frequency and severity of hot flushes during the treatment period. The baseline assessment for hot flushes was calculated using the last 7 days (not necessarily consecutive days) with an available data in the evening and/or the morning of the baseline diary completion period. A diary day was comprised of the evening entry of this day and the morning entry of the following day, in that order. Mean daily frequency = Sum of number of hot flushes filled in the diary during the last 7 diary days (with at least one available data in the evening and/or morning) divided by 7. Moderate: Sensation of heat with sweating, but able to continue activity. Severe: Sensation of heat with sweating, causing cessation (stopping) of activity. In categories the number of subjects analyzed (N) at week 12 is mentioned for each reporting group respectively.	
End point type	Primary
End point timeframe: Week 12	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	11.82 (± 4.42)	12.13 (± 8.81)	14.55 (± 5.87)	13.54 (± 7.17)
Week 12: Change from baseline (N=44,30,16,51,43)	-4.49 (± 4.29)	-6.48 (± 7.82)	-5.49 (± 5.31)	-7.91 (± 6.66)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	12.92 (± 6.90)			
Week 12: Change from baseline (N=44,30,16,51,43)	-6.57 (± 5.83)			

**Statistical analyses**

Statistical analysis title	40 mg BAY3427080 versus placebo
Comparison groups	Placebo v 40 mg BAY3427080

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2097
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.28
upper limit	-0.95

<b>Statistical analysis title</b>	80 mg BAY3427080 versus placebo
Comparison groups	Placebo v 80 mg BAY3427080
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6369
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.97
upper limit	2.44

<b>Statistical analysis title</b>	120 mg BAY3427080 versus placebo
Comparison groups	Placebo v 120 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0116
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-2.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.22
upper limit	-0.67

<b>Statistical analysis title</b>	160 mg BAY3427080 versus placebo
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Comparison groups	Placebo v 160 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1346
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	0.56

### Primary: Mean change from baseline in mean severity of moderate and severe hot flushes from baseline to Week 4

End point title	Mean change from baseline in mean severity of moderate and severe hot flushes from baseline to Week 4
End point description:	Subjects recorded daily in their eDiary the frequency and severity of hot flushes during the treatment period. Mean weekly severity = (number of moderate hot flushes for 7 days) x 2 + (number of severe hot flushes for 7 days) x 3] / (total number of moderate to severe hot flushes over 7 days). Severity is graded by the women from 1 to 3 (1 = mild; 2 = moderate; 3 = severe). In categories the number of subjects analyzed (N) at week 4 is mentioned for each reporting group respectively.
End point type	Primary
End point timeframe:	
From baseline to week 4	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	2.54 (± 0.20)	2.51 (± 0.26)	2.63 (± 0.24)	2.54 (± 0.24)
Week 4: Change from baseline (N=45,31,17,50,45)	-0.31 (± 0.41)	-0.38 (± 0.54)	-0.44 (± 0.56)	-0.52 (± 0.58)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	2.54 (± 0.26)			

Week 4: Change from baseline (N=45,31,17,50,45)	-0.55 ( $\pm$ 0.68)			
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### Statistical analyses

<b>Statistical analysis title</b>	40 mg BAY3427080 versus placebo
Comparison groups	Placebo v 40 mg BAY3427080
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7033
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.2

<b>Statistical analysis title</b>	80 mg BAY3427080 versus placebo
Comparison groups	Placebo v 80 mg BAY3427080
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3724
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.17

<b>Statistical analysis title</b>	120 mg BAY3427080 versus placebo
Comparison groups	Placebo v 120 mg BAY3427080

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0896
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.03

<b>Statistical analysis title</b>	160 mg BAY3427080 versus placebo
Comparison groups	Placebo v 160 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.03

### **Primary: Mean change from baseline in mean severity of moderate and severe hot flushes from baseline to Week 12**

End point title	Mean change from baseline in mean severity of moderate and severe hot flushes from baseline to Week 12
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#### End point description:

Subjects recorded daily in their eDiary the frequency and severity of hot flushes during the treatment period. Mean weekly severity = (number of moderate hot flushes for 7 days) x 2 + (number of severe hot flushes for 7 days) x 3] / (total number of moderate to severe hot flushes over 7 days). Severity was graded by the women from 1 to 3 (1 = mild; 2 = moderate; 3 = severe).

In categories the number of subjects analyzed (N) at week 12 is mentioned for each reporting group respectively.

End point type	Primary
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End point timeframe:

Week 12



<b>End point values</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	2.54 (± 0.20)	2.51 (± 0.26)	2.63 (± 0.24)	2.54 (± 0.24)
Week 12: Change from baseline (N=44,30,16,49,41)	-0.41 (± 0.50)	-0.53 (± 0.64)	-0.26 (± 0.45)	-0.56 (± 0.68)

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	2.54 (± 0.26)			
Week 12: Change from baseline (N=44,30,16,49,41)	-0.73 (± 0.78)			

## Statistical analyses

<b>Statistical analysis title</b>	40 mg BAY3427080 versus placebo
Comparison groups	Placebo v 40 mg BAY3427080
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5511
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	0.21

<b>Statistical analysis title</b>	80 mg BAY3427080 versus placebo
Comparison groups	Placebo v 80 mg BAY3427080

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3822
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.52

<b>Statistical analysis title</b>	120 mg BAY3427080 versus placebo
Comparison groups	Placebo v 120 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2606
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.11

<b>Statistical analysis title</b>	160 mg BAY3427080 versus placebo
Comparison groups	Placebo v 160 mg BAY3427080
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0479
Method	Mixed-Effect Model Repeated Measures
Parameter estimate	Difference in LS means
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0

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## Secondary: Mean change from baseline in frequency of mean daily moderate and

**severe hot flushes from baseline to Weeks 1, 2, 8 and 16**

End point title	Mean change from baseline in frequency of mean daily moderate and severe hot flushes from baseline to Weeks 1, 2, 8 and 16
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## End point description:

Subjects recorded daily in their electronic diary (eDiary) the frequency and severity of hot flushes during the treatment period. The baseline assessment for hot flushes was calculated using the last 7 days (not necessarily consecutive days) with an available data in the evening and/or the morning of the baseline diary completion period. A diary day was comprised of the evening entry of this day and the morning entry of the following day, in that order. Mean daily frequency = Sum of number of hot flushes filled in the diary during the last 7 diary days (with at least one available data in the evening and/or morning) divided by 7. Moderate: Sensation of heat with sweating, but able to continue activity. Severe: Sensation of heat with sweating, causing cessation (stopping) of activity  
In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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## End point timeframe:

From baseline to Weeks 1, 2, 8 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	11.82 (± 4.42)	12.13 (± 8.81)	14.55 (± 5.87)	13.54 (± 7.17)
Week 1: Change from baseline (N=47,31,17,52,52)	-1.22 (± 3.07)	-1.61 (± 3.05)	-1.63 (± 3.56)	-3.22 (± 3.43)
Week 2: Change from baseline (N=45,31,17,52,51)	-2.19 (± 4.01)	-3.03 (± 3.95)	-3.47 (± 4.37)	-4.58 (± 4.70)
Week 8: Change from baseline (N=44,31,17,51,44)	-4.33 (± 4.79)	-5.72 (± 6.18)	-5.94 (± 5.26)	-7.84 (± 5.95)
Week 16: Change from baseline (N=43,30,16,51,42)	-3.95 (± 4.85)	-5.74 (± 9.45)	-2.01 (± 4.99)	-5.95 (± 6.95)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	12.92 (± 6.90)			
Week 1: Change from baseline (N=47,31,17,52,52)	-3.09 (± 3.76)			
Week 2: Change from baseline (N=45,31,17,52,51)	-3.78 (± 4.48)			
Week 8: Change from baseline (N=44,31,17,51,44)	-5.58 (± 6.00)			
Week 16: Change from baseline (N=43,30,16,51,42)	-2.78 (± 6.54)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean change from baseline in mean severity of moderate and severe hot flushes from baseline to Weeks 1, 2, 8 and 16

End point title	Mean change from baseline in mean severity of moderate and severe hot flushes from baseline to Weeks 1, 2, 8 and 16
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End point description:

Subjects recorded daily in their diary the frequency and severity of hot flushes during the treatment period. Mean weekly severity = (number of moderate hot flushes for 7 days) x 2 + (number of severe hot flushes for 7 days) x 3] / (total number of moderate to severe hot flushes over 7 days). Severity is graded by the women from 1 to 3 (1 = mild; 2 = moderate; 3 = severe). In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 1, 2, 8 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	50
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,50,50)	2.54 (± 0.20)	2.51 (± 0.26)	2.63 (± 0.24)	2.54 (± 0.24)
Week 1: Change from baseline (N=47,31,17,50,50)	-0.24 (± 0.30)	-0.21 (± 0.20)	-0.22 (± 0.21)	-0.25 (± 0.28)
Week 2: Change from baseline (N=45,31,17,50,49)	-0.30 (± 0.39)	-0.32 (± 0.32)	-0.42 (± 0.58)	-0.37 (± 0.46)
Week 8: Change from baseline (N=44,31,17,50,42)	-0.45 (± 0.58)	-0.48 (± 0.54)	-0.40 (± 0.61)	-0.51 (± 0.54)
Week 16: Change from baseline (N=43,30,16,49,41)	2.15 (± 0.65)	2.03 (± 0.56)	2.50 (± 0.46)	2.13 (± 0.71)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,50,50)	2.55 (± 0.26)			
Week 1: Change from baseline (N=47,31,17,50,50)	-0.26 (± 0.26)			

Week 2: Change from baseline (N=45,31,17,50,49)	-0.40 (± 0.55)			
Week 8: Change from baseline (N=44,31,17,50,42)	-0.65 (± 0.73)			
Week 16: Change from baseline (N=43,30,16,49,41)	2.08 (± 0.62)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean change from baseline in mean daily frequency of all hot flushes from baseline to Weeks 1, 2, 4, 8, 12 and 16

End point title	Mean change from baseline in mean daily frequency of all hot flushes from baseline to Weeks 1, 2, 4, 8, 12 and 16
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End point description:

Subjects recorded daily in their electronic diary (eDiary) the frequency and severity of hot flushes during the treatment period. The baseline assessment for hot flushes was calculated using the last 7 days (not necessarily consecutive days) with an available data in the evening and/or the morning of the baseline diary completion period. A diary day was comprised of the evening entry of this day and the morning entry of the following day, in that order. Mean daily frequency = Sum of number of hot flushes filled in the diary during the last 7 diary days (with at least one available data in the evening and/or morning) divided by 7. Moderate: Sensation of heat with sweating, but able to continue activity. Severe: Sensation of heat with sweating, causing cessation (stopping) of activity.

\*In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	14.04 (± 5.57)	14.19 (± 11.01)	16.55 (± 6.89)	15.39 (± 7.91)
Week 1 (N=47,31,17,52,52)	-1.36 (± 3.03)	-1.72 (± 3.27)	-1.33 (± 5.68)	-3.30 (± 3.99)
Week 2 (N=45,31,17,52,51)	-2.35 (± 4.60)	-2.99 (± 4.90)	-2.74 (± 5.97)	-4.57 (± 5.48)
Week 4 (N=45,31,17,52,47)	-2.67 (± 4.09)	-4.11 (± 6.31)	-3.45 (± 8.54)	-6.70 (± 6.16)
Week 8 (N=44,31,17,51,44)	-4.74 (± 5.57)	-5.65 (± 6.55)	-5.45 (± 6.56)	-7.96 (± 6.16)
Week 12 (N=44,30,16,51,43)	-5.07 (± 5.48)	-6.50 (± 8.67)	-5.11 (± 8.41)	-7.94 (± 6.74)
Week 16 (N=43,30,16,51,42)	-4.60 (± 6.17)	-5.83 (± 10.86)	-1.76 (± 7.50)	-6.19 (± 7.68)

End point values	160 mg BAY3427080			
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Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	15.78 (± 9.62)			
Week 1 (N=47,31,17,52,52)	-3.69 (± 4.81)			
Week 2 (N=45,31,17,52,51)	-4.43 (± 5.68)			
Week 4 (N=45,31,17,52,47)	-5.79 (± 6.09)			
Week 8 (N=44,31,17,51,44)	-6.03 (± 6.43)			
Week 12 (N=44,30,16,51,43)	-7.47 (± 7.13)			
Week 16 (N=43,30,16,51,42)	-3.11 (± 6.71)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in mean severity of all hot flushes from baseline to Weeks 1, 2, 4, 8, 12 and 16

End point title	Mean change from baseline in mean severity of all hot flushes from baseline to Weeks 1, 2, 4, 8, 12 and 16
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End point description:

Subjects recorded daily in their diary the frequency and severity of hot flushes during the treatment period. Mean weekly severity = (number of moderate hot flushes for 7 days) x 2 + (number of severe hot flushes for 7 days) x 3] / (total number of moderate to severe hot flushes over 7 days). Severity is graded by the women from 1 to 3 (1 = mild; 2 = moderate; 3 = severe).

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	2.34 (± 0.32)	2.34 (± 0.35)	2.46 (± 0.37)	2.38 (± 0.34)
Week 1: Change from baseline (N=47,31,17,52,52)	-0.04 (± 0.23)	-0.04 (± 0.18)	-0.05 (± 0.12)	-0.09 (± 0.25)
Week 2: Change from baseline (N=45,31,17,52,51)	-0.10 (± 0.32)	-0.15 (± 0.27)	-0.25 (± 0.52)	-0.21 (± 0.46)
Week 4: Change from baseline (N=45,31,17,52,47)	-0.11 (± 0.36)	-0.21 (± 0.47)	-0.27 (± 0.49)	-0.35 (± 0.60)
Week 8: Change from baseline (N=44,31,17,51,44)	-0.25 (± 0.54)	-0.31 (± 0.47)	-0.23 (± 0.52)	-0.35 (± 0.55)
Week 12: Change from baseline (N=44,30,16,51,43)	-0.21 (± 0.44)	-0.35 (± 0.57)	-0.08 (± 0.41)	-0.41 (± 0.62)
Week 16: Change from baseline (N=43,30,16,51,42)	-0.21 (± 0.49)	-0.30 (± 0.52)	0.05 (± 0.34)	-0.26 (± 0.56)

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Hot Flushes				
arithmetic mean (standard deviation)				
Baseline	2.35 (± 0.39)			
Week 1: Change from baseline (N=47,31,17,52,52)	-0.07 (± 0.18)			
Week 2: Change from baseline (N=45,31,17,52,51)	-0.20 (± 0.50)			
Week 4: Change from baseline (N=45,31,17,52,47)	-0.34 (± 0.63)			
Week 8: Change from baseline (N=44,31,17,51,44)	-0.44 (± 0.72)			
Week 12: Change from baseline (N=44,30,16,51,43)	-0.52 (± 0.79)			
Week 16: Change from baseline (N=43,30,16,51,42)	-0.24 (± 0.54)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in the mean daily hot flush score (frequency x severity) at Weeks 1, 2, 4, 8, 12 and 16

End point title	Mean change from baseline in the mean daily hot flush score (frequency x severity) at Weeks 1, 2, 4, 8, 12 and 16
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End point description:

Mean daily Hot Flushes score = Sum of (frequency x severity) filled in the diary during the last 7 days (with at least one available data in the evening and/or morning) divided by 7. Severity is graded by the women from 1 to 3 (1 = mild; 2 = moderate; 3 = severe).

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12 and 16

<b>End point values</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	32.35 (± 12.24)	32.84 (± 24.82)	40.76 (± 17.08)	36.59 (± 19.88)
Week 1: Change from baseline (N=47,31,17,52,52)	-3.09 (± 8.16)	-4.26 (± 7.93)	-4.18 (± 11.27)	-8.44 (± 8.98)

Week 2: Change from baseline (N=45,31,17,52,51)	-5.62 (± 11.00)	-7.88 (± 10.77)	-9.08 (± 13.09)	-11.98 (± 12.39)
Week 4: Change from baseline (N=45,31,17,52,47)	-6.62 (± 9.79)	-10.68 (± 15.26)	-11.39 (± 18.82)	-17.54 (± 15.50)
Week 8: Change from baseline (N=44,31,17,51,44)	-11.63 (± 12.51)	-14.64 (± 16.33)	-16.17 (± 15.32)	-20.54 (± 15.80)
Week 12: Change from baseline (N=44,30,16,51,43)	-12.33 (± 11.96)	-16.71 (± 20.60)	-14.93 (± 16.83)	-20.72 (± 17.81)
Week 16: Change from baseline (N=43,30,16,51,42)	-10.89 (± 13.45)	-14.93 (± 25.48)	-4.97 (± 14.35)	-15.60 (± 19.03)

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	35.73 (± 19.75)			
Week 1: Change from baseline (N=47,31,17,52,52)	-8.67 (± 10.53)			
Week 2: Change from baseline (N=45,31,17,52,51)	-10.51 (± 12.47)			
Week 4: Change from baseline (N=45,31,17,52,47)	-14.20 (± 14.30)			
Week 8: Change from baseline (N=44,31,17,51,44)	-14.89 (± 15.36)			
Week 12: Change from baseline (N=44,30,16,51,43)	-17.70 (± 15.38)			
Week 16: Change from baseline (N=43,30,16,51,42)	-7.50 (± 16.55)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with ≥50% and ≥80% reduction from baseline in mean daily hot flushes frequency at Week 12

End point title	Number of subjects with ≥50% and ≥80% reduction from baseline in mean daily hot flushes frequency at Week 12
End point description:	
Proportion of responder is number of subjects with >=50 (80)% reduction from baseline in the number of moderate and severe hot flushes.	
End point type	Secondary
End point timeframe:	
Week 12	



End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
>= 50% reduction	17	20	5	32
>=80% reduction	8	6	0	16

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
>= 50% reduction	30			
>=80% reduction	18			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in number of all night-time awakenings (NTA) at Weeks 1, 2, 4, 8, 12 and 16

End point title	Mean change from baseline in number of all night-time awakenings (NTA) at Weeks 1, 2, 4, 8, 12 and 16
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End point description:

Subjects were provided with an eDiary to document the number of night-time awakenings (NTA). Each evening, subjects recorded the total number of hot flushes of each severity experienced that day since waking. Each morning upon waking, subjects recorded the number of times they woke up in the night and the total number of hot flushes of each severity experienced during the night. In categories the number of subjects analyzed (N) at each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to weeks 1, 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	51
Units: Night-time awakenings				
arithmetic mean (standard deviation)				
Baseline	3.86 (± 2.06)	3.44 (± 1.82)	5.00 (± 1.76)	3.80 (± 2.20)
Week 1: Change from baseline (N=47,31,17,52,52)	-0.65 (± 1.08)	-0.70 (± 1.24)	-0.57 (± 1.57)	-0.91 (± 1.06)
Week 2: Change from baseline (N=45,31,17,52,51)	-0.62 (± 1.54)	-0.70 (± 1.20)	-1.09 (± 1.84)	-1.10 (± 1.34)
Week 4: Change from baseline (N=45,31,17,52, 47)	-0.86 (± 1.40)	-1.05 (± 1.43)	-0.99 (± 2.96)	-1.49 (± 1.43)

Week 8: Change from baseline (N=44,31,17,51,44)	-0.99 (± 1.31)	-1.66 (± 1.77)	-1.30 (± 2.15)	-1.79 (± 1.47)
Week 12: Change from baseline (N=44,30,16,51,43)	-1.28 (± 1.44)	-1.53 (± 1.89)	-1.61 (± 2.46)	-1.60 (± 1.38)
Week 16: Change from baseline (N=43,30,16,51,42)	-1.08 (± 1.30)	-0.96 (± 1.91)	-0.31 (± 2.90)	-1.05 (± 1.30)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Night-time awakenings				
arithmetic mean (standard deviation)				
Baseline	3.85 (± 2.57)			
Week 1: Change from baseline (N=47,31,17,52,52)	-0.86 (± 1.93)			
Week 2: Change from baseline (N=45,31,17,52,51)	-1.00 (± 2.10)			
Week 4: Change from baseline (N=45,31,17,52, 47)	-1.03 (± 2.22)			
Week 8: Change from baseline (N=44,31,17,51,44)	-1.17 (± 2.51)			
Week 12: Change from baseline (N=44,30,16,51,43)	-1.40 (± 2.40)			
Week 16: Change from baseline (N=43,30,16,51,42)	-0.32 (± 2.10)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in mean daily number of NTAs secondary to hot flushes at Weeks 1, 2, 4, 8, 12 and 16

End point title	Mean change from baseline in mean daily number of NTAs secondary to hot flushes at Weeks 1, 2, 4, 8, 12 and 16
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End point description:

Subjects were provided with an eDiary to document the number of night-time awakenings (NTA). Each evening, subjects recorded the total number of hot flashes of each severity experienced that day since waking. Each morning upon waking, subjects recorded the number of times they woke up in the night and the total number of hot flashes of each severity experienced during the night. Night-time awakenings secondary to hot flashes corresponded to severe hot flash recorded on the morning diary, and all NTAs corresponded to the data recorded in the "Total number of times you woke up last night?" field from the eDiary recorded in the morning. Number of NTAs secondary to hot flushes could not be higher than the number of all NTAs.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 1, 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Night-time awakenings				
arithmetic mean (standard deviation)				
Baseline	2.90 (± 1.64)	2.41 (± 1.57)	4.05 (± 1.86)	2.76 (± 1.71)
Week 1: Change from baseline (N=47,31,17,52,52)	-0.57 (± 0.96)	-0.52 (± 1.07)	-0.63 (± 1.53)	-0.90 (± 1.03)
Week 2: Change from baseline (N=45,31,17,52,51)	-0.69 (± 1.03)	-0.75 (± 1.18)	-1.13 (± 1.89)	-1.18 (± 1.27)
Week 4: Change from baseline (N=45,31,17,52,47)	-0.89 (± 1.08)	-0.91 (± 1.26)	-1.33 (± 2.27)	-1.53 (± 1.19)
Week 8: Change from baseline (N=44,31,17,51,44)	-1.09 (± 1.36)	-1.50 (± 1.40)	-1.69 (± 2.21)	-1.79 (± 1.35)
Week 12: Change from baseline (N=44,30,16,51,43)	-1.31 (± 1.39)	-1.63 (± 1.46)	-1.70 (± 2.53)	-1.67 (± 1.27)
Week 16: Change from baseline (N=43,30,16,51,42)	-1.05 (± 1.19)	-1.29 (± 1.63)	-0.45 (± 2.05)	-1.19 (± 1.23)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Night-time awakenings				
arithmetic mean (standard deviation)				
Baseline	2.57 (± 1.54)			
Week 1: Change from baseline (N=47,31,17,52,52)	-0.68 (± 1.14)			
Week 2: Change from baseline (N=45,31,17,52,51)	-0.92 (± 1.38)			
Week 4: Change from baseline (N=45,31,17,52,47)	-1.01 (± 1.62)			
Week 8: Change from baseline (N=44,31,17,51,44)	-1.13 (± 1.86)			
Week 12: Change from baseline (N=44,30,16,51,43)	-1.32 (± 1.75)			
Week 16: Change from baseline (N=43,30,16,51,42)	-0.44 (± 1.62)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in the global and individual domain scores of the Pittsburgh Sleep Quality Index (PSQI) at Weeks 4, 8, 12 and 16

End point title	Change from baseline in the global and individual domain scores of the Pittsburgh Sleep Quality Index (PSQI) at Weeks 4, 8, 12 and 16
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End point description:

The PSQI is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval. Nineteen individual items generate seven "component" scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication,

and daytime dysfunction. The sum of scores for these seven components yields one global score. In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
End point timeframe:	
From baseline to Weeks 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=45,31,17,51,50)	10.80 (± 2.39)	11.94 (± 3.11)	11.35 (± 3.66)	10.80 (± 3.00)
Week 4: Change from baseline (N=41,31,17,50,45)	-0.63 (± 2.02)	-1.87 (± 2.93)	-1.94 (± 2.68)	-2.70 (± 3.11)
Week 8: Change from baseline (N=42,31,16,51,43)	-1.36 (± 2.90)	-2.39 (± 3.63)	-2.38 (± 3.30)	-3.00 (± 3.23)
Week 12: Change from baseline (N=41,30,16,49,41)	-1.15 (± 2.95)	-2.47 (± 3.82)	-2.81 (± 2.97)	-3.39 (± 3.12)
Week 16: Change from baseline (N=41,30,16,50,42)	-1.85 (± 2.46)	-2.10 (± 3.53)	-1.38 (± 3.26)	-2.24 (± 3.12)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=45,31,17,51,50)	11.44 (± 3.14)			
Week 4: Change from baseline (N=41,31,17,50,45)	-2.80 (± 2.84)			
Week 8: Change from baseline (N=42,31,16,51,43)	-3.14 (± 3.37)			
Week 12: Change from baseline (N=41,30,16,49,41)	-3.54 (± 4.12)			
Week 16: Change from baseline (N=41,30,16,50,42)	-1.79 (± 2.69)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in the Insomnia Severity Index (ISI) score at Weeks 4, 8, 12 and 16

End point title	Change from baseline in the Insomnia Severity Index (ISI) score at Weeks 4, 8, 12 and 16
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**End point description:**

The ISI is a brief self-report questionnaire assessing the nature, severity, and impact of insomnia. The ISI comprises seven items assessing the perceived severity of difficulties initiating sleep, staying asleep, and early morning awakenings, satisfaction with current sleep pattern, interference with daily functioning, noticeability of impairment attributed to the sleep problem, and degree of distress or concern caused by the sleep problem. Subjects rated each item on a scale of 0 to 4, yielding a total score ranging from 0 to 28.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
End point timeframe:	
From baseline to Weeks 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=44,31,17,51,50)	12.43 (± 5.09)	13.23 (± 5.36)	13.24 (± 8.04)	12.63 (± 5.66)
Week 4: Change from Baseline (N=40,31,17,50,45)	-1.60 (± 2.98)	-2.74 (± 4.91)	-3.65 (± 6.03)	-5.14 (± 5.51)
Week 8: Change from Baseline (N=41,31,16,51,43)	-1.51 (± 3.64)	-3.74 (± 5.63)	-4.44 (± 6.17)	-6.20 (± 4.93)
Week 12: Change from Baseline (N=40,30,16, 49,41)	-1.95 (± 4.70)	-3.80 (± 5.45)	-5.81 (± 5.86)	-6.12 (± 5.41)
Week 16: Change from Baseline (N=40,30,16,50,42)	-2.65 (± 4.32)	-3.73 (± 6.02)	-3.00 (± 3.72)	-4.34 (± 5.58)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=44,31,17,51,50)	13.74 (± 5.89)			
Week 4: Change from Baseline (N=40,31,17,50,45)	-5.42 (± 5.42)			
Week 8: Change from Baseline (N=41,31,16,51,43)	-5.72 (± 5.14)			
Week 12: Change from Baseline (N=40,30,16, 49,41)	-7.39 (± 5.82)			
Week 16: Change from Baseline (N=40,30,16,50,42)	-4.00 (± 5.49)			

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Change from baseline in the hot flush related daily interference scale (HFRDIS) scores at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in the hot flush related daily interference scale (HFRDIS) scores at Weeks 2, 4, 8, 12 and 16
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End point description:

The HFRDIS is a 10-item, self-report questionnaire assessing the impact of hot flashes on a woman's life during the past week. For each of the 10 items, subjects rated how much hot flushes had interfered with that aspect of their life on a scale of 0 (not at all) to 10 (very much so).

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=45,31,17,51,50)	52.93 (± 18.40)	52.74 (± 20.33)	50.29 (± 21.45)	53.86 (± 23.42)
Week 2: Change from baseline (N=42,31,17,51,48)	-4.00 (± 20.28)	-5.39 (± 21.99)	-11.12 (± 28.14)	-13.75 (± 29.66)
Week 4: Change from baseline (N=43,31,17,50,45)	-9.98 (± 20.84)	-13.00 (± 22.53)	-15.06 (± 24.02)	-23.04 (± 28.32)
Week 8: Change from baseline (N=42,31,16,51,43)	-15.48 (± 21.07)	-16.26 (± 23.71)	-17.88 (± 27.15)	-26.39 (± 24.90)
Week 12: Change from baseline (N=41,30,16,49,41)	-19.37 (± 20.20)	-21.30 (± 22.89)	-15.56 (± 28.70)	-28.33 (± 25.36)
Week 16: Change from baseline (N=41,30,16,50,42)	-15.22 (± 21.72)	-10.73 (± 24.87)	-16.69 (± 24.15)	-19.16 (± 22.43)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=45,31,17,51,50)	55.36 (± 19.71)			
Week 2: Change from baseline (N=42,31,17,51,48)	-10.90 (± 21.31)			
Week 4: Change from baseline (N=43,31,17,50,45)	-18.44 (± 23.37)			
Week 8: Change from baseline (N=42,31,16,51,43)	-24.09 (± 25.51)			
Week 12: Change from baseline (N=41,30,16,49,41)	-27.83 (± 24.64)			
Week 16: Change from baseline (N=41,30,16,50,42)	-12.07 (± 25.94)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in the Menopause-specific Quality-of-Life questionnaire Intervention Version (MenQoL-I) scores at Weeks 4, 8, 12 and 16

End point title	Change from baseline in the Menopause-specific Quality-of-Life questionnaire Intervention Version (MenQoL-I) scores at Weeks 4, 8, 12 and 16
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End point description:

The MenQoL-I is a validated questionnaire used to measure condition-specific quality of life in menopausal women. It is composed of 32 items across four domains (physical, vasomotor, psychosocial and sexual). For each item, subjects recorded whether they had experienced the problem in the past month, and if so, they rated how bothered they were by the problem on a scale of 0 (not at all bothered) to 6 (extremely bothered). The item responses were then converted into analysis scores and an overall questionnaire score.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 4, 8, 12 and 16;

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=46,31,17,51,51)	4.00 (± 1.06)	4.38 (± 1.16)	4.47 (± 1.25)	4.17 (± 1.13)
Week 4: Change from baseline (N=42,31,17,50,46)	-0.33 (± 0.90)	-0.62 (± 1.30)	-0.56 (± 0.87)	-1.29 (± 1.14)
Week 8: Change from baseline (N=43,31,16,51,43)	-0.62 (± 1.10)	-0.87 (± 1.25)	-0.91 (± 1.06)	-1.45 (± 1.18)
Week 12: Change from baseline (N=42,30,16,49,41)	-0.70 (± 1.03)	-0.81 (± 1.44)	-1.09 (± 0.76)	-1.54 (± 1.34)
Week 16: Change from baseline (N=42,30,16,50,42)	-0.68 (± 1.01)	-0.76 (± 1.33)	-0.69 (± 0.93)	-1.18 (± 1.13)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Scores on scale				
arithmetic mean (standard deviation)				

Baseline (N=46,31,17,51,51)	4.50 ( $\pm$ 1.23)			
Week 4: Change from baseline (N=42,31,17,50,46)	-1.13 ( $\pm$ 1.09)			
Week 8: Change from baseline (N=43,31,16,51,43)	-1.50 ( $\pm$ 0.99)			
Week 12: Change from baseline (N=42,30,16,49,41)	-1.72 ( $\pm$ 1.32)			
Week 16: Change from baseline (N=42,30,16,50,42)	-1.00 ( $\pm$ 1.36)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in the Beck Depression Inventory II (BDI-II) scores at Weeks 2, 4, 8, 12 and 16.

End point title	Change from baseline in the Beck Depression Inventory II (BDI-II) scores at Weeks 2, 4, 8, 12 and 16.
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End point description:

The BDI-II is a 21-item questionnaire assessing the intensity of depressive symptoms over the past 2 weeks. It is composed of items relating to symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. Subjects rated each item on a scale of 0 to 3 to give a total score ranging from 0 to 63, with a higher score suggesting more severe depressive symptoms. In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=44,31,17,51,50)	11.18 ( $\pm$ 8.74)	14.29 ( $\pm$ 11.36)	10.47 ( $\pm$ 7.01)	9.92 ( $\pm$ 8.62)
Week 2: Change from baseline (N=41,31,17,51,48)	-1.90 ( $\pm$ 5.29)	-2.23 ( $\pm$ 9.27)	-3.06 ( $\pm$ 7.34)	-3.65 ( $\pm$ 6.95)
Week 4: Change from baseline (N=42,31,17,50,45)	-1.55 ( $\pm$ 5.14)	-4.23 ( $\pm$ 9.82)	-2.35 ( $\pm$ 5.16)	-4.08 ( $\pm$ 6.39)
Week 8: Change from baseline (N=41,31,16,51,43)	-2.24 ( $\pm$ 5.26)	-5.32 ( $\pm$ 10.13)	-2.00 ( $\pm$ 8.22)	-4.73 ( $\pm$ 6.34)
Week 12: Change from baseline (N=40,30,16,49,41)	-1.30 ( $\pm$ 7.22)	-5.00 ( $\pm$ 3.80)	-1.69 ( $\pm$ 7.65)	-4.29 ( $\pm$ 6.56)
Week 16: Change from baseline (N=40,30,16,50,42)	-2.43 ( $\pm$ 6.08)	-5.10 ( $\pm$ 11.62)	-0.75 ( $\pm$ 6.71)	-4.04 ( $\pm$ 6.12)



<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (N=44,31,17,51,50)	11.48 (± 9.30)			
Week 2: Change from baseline (N=41,31,17,51,48)	-2.71 (± 6.08)			
Week 4: Change from baseline (N=42,31,17,50,45)	-4.13 (± 6.63)			
Week 8: Change from baseline (N=41,31,16,51,43)	-5.51 (± 7.14)			
Week 12: Change from baseline (N=40,30,16,49,41)	-5.73 (± 7.39)			
Week 16: Change from baseline (N=40,30,16,50,42)	-2.36 (± 8.05)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma BAY3427080 Concentrations at Weeks 2, 4, 8 ,12

End point title	Plasma BAY3427080 Concentrations at Weeks 2, 4, 8 ,12 <sup>[1]</sup>
End point description:	
Blood samples for analysis of plasma BAY3427080 concentrations were collected at Weeks 2, 4, 8, and 12.	
A small number of subjects had NT-814 concentrations below the LOQ for the assay (1.5 ng/mL) at two or more visits (three subjects in each of the 40 mg, 120 mg, and 160 mg groups, four in 80 mg group), indicating that these subjects were non compliant with treatment.	
End point type	Secondary
End point timeframe:	
At weeks 2, 4, 8 ,12	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: PK samples were collected for placebo subjects but not analyzed. Only subjects who received the active study drug and for whom valid PK data were available were included in the pharmacokinetic analysis.

<b>End point values</b>	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080	160 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31 <sup>[2]</sup>	17 <sup>[3]</sup>	52 <sup>[4]</sup>	52 <sup>[5]</sup>
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Week 2	64.254 (± 75.681)	157.207 (± 93.120)	292.929 (± 100.381)	319.552 (± 170.571)
Week 4	78.946 (± 78.892)	118.554 (± 175.865)	253.800 (± 142.944)	398.389 (± 91.644)
Week 8	87.985 (± 68.277)	138.795 (± 72.619)	226.121 (± 79.171)	341.673 (± 145.535)
Week 12	70.138 (± 66.542)	130.729 (± 414.199)	197.041 (± 231.390)	298.896 (± 220.963)

Notes:

[2] - Safety Analysis Set

[3] - Safety Analysis Set

[4] - Safety Analysis Set

[5] - Safety Analysis Set

## Statistical analyses

No statistical analyses for this end point

## Secondary: Nature and severity of adverse events

End point title	Nature and severity of adverse events
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End point description:

A Treatment-Emergent Adverse Events (TEAE) is defined as any adverse event (serious and non-serious) with the onset date on or after the date of first dosing with study treatment. Safety Analysis Set.

End point type	Secondary
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End point timeframe:

Up to Week 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Number of TEAEs	28	17	14	34
Number of TEAEs related to IMP	7	7	8	8
Number of Serious TEAEs	2	0	1	1
Number of TEAEs leading to death	0	0	0	0
Number of Severe TEAEs	2	0	1	3

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Number of TEAEs	38			
Number of TEAEs related to IMP	12			
Number of Serious TEAEs	1			
Number of TEAEs leading to death	0			
Number of Severe TEAEs	2			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Withdrawals due to an adverse event

End point title	Withdrawals due to an adverse event
End point description: A Treatment-Emergent Adverse Events (TEAE) is defined as any adverse event (serious and non-serious) with the onset date on or after the date of first dosing with study treatment.	
End point type	Secondary
End point timeframe: Up to Week 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
TEAEs leading to treatment discontinuation	1	0	2	0
TEAEs leading to study discontinuation	1	0	1	0

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
TEAEs leading to treatment discontinuation	5			
TEAEs leading to study discontinuation	4			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects used concomitant medications

End point title	Number of subjects used concomitant medications
End point description: A concomitant medication is defined as any medication used on or after date and time of first randomised treatment. All concomitant medications taken during the study were recorded in the eCRF. Any medication that was not specifically prohibited was allowed. (1) Antidiarrheals, intestinal antiinflammatory/antiinfective agents;	
End point type	Secondary
End point timeframe: Up to week 16	

<b>End point values</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Analgesics	18	8	9	12
Antiinflammatory and antirheumatic products	14	7	5	12
Vitamins	14	6	6	9
Drugs for acid related disorders	13	7	2	10
Psychoanaleptics	6	5	4	10
Psycholeptics	3	7	5	7
Antibacterials for systemic use	9	5	2	5
Drugs for obstructive airway diseases	7	3	3	4
Lipid modifying agents	3	3	4	8
Agents acting on the renin-angiotensin system	7	4	0	11
Thyroid therapy	4	3	3	7
Antihistamines for systemic use	5	4	3	6
Antithrombotic agents	2	4	2	6
Nasal preparations	2	4	1	1
Diuretics	1	2	0	5
Antianemic preparations	5	2	2	5
Mineral supplements	2	2	3	3
Calcium channel blockers	3	0	1	6
Drugs used in diabetes	3	2	0	1
Beta blocking agents	1	2	0	5
Ophthalmologicals	1	1	2	3
Urologicals	1	1	1	3
Antidiarrheals, intestinal agents (1)	2	2	0	0
Antivirals for systemic use	1	3	1	1
Corticosteroids for systemic use	1	1	0	1
Drugs for constipation	2	0	1	3
Anesthetics	0	1	0	3
Antiemetics and antinauseants	2	0	1	1
Drugs for functional gastrointestinal disorders	3	1	0	1
General nutrients	1	1	0	1
Topical products for joint and muscular pain	1	2	0	0
Antifungals for dermatological use	0	1	1	0
Antiobesity preparations, excl. Diet products	0	0	0	2
Corticosteroids, dermatological preparations	1	2	0	1
Cough and cold preparations	3	1	0	2
Other nervous system drugs	1	1	0	1
Unspecified herbal and traditional medicine	1	0	1	1
All other therapeutic products	0	1	0	1
Anti-acne preparations	0	1	0	1

Other alimentary tract and metabolism products	1	1	0	1
Throat preparations	0	1	0	0
Vaccines	0	1	0	1
Antiepileptics	0	0	1	0
Antihemorrhagics	0	0	0	0
Antihypertensives	0	0	1	0
Antiprotozoals	0	0	0	0
Antipruritics, incl. antihistamines, anesthetics	0	0	0	0
Antipsoriatics	0	0	0	0
Bile and liver therapy	0	0	0	1
Drugs for treatment of bone diseases	0	0	1	0
Gynecological antiinfectives and antiseptics	0	0	0	1
Immunosuppressants	0	0	0	1
Other respiratory system products	0	0	0	0
Stomatological preparations	0	0	0	0
Tonics	0	0	0	1
Muscle relaxants	2	0	1	1
Antibiotics,chemotherapeutics (dermatological use)	1	0	0	1
Antimycotics for systemic use	1	0	0	0

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Analgesics	16			
Antiinflammatory and antirheumatic products	13			
Vitamins	14			
Drugs for acid related disorders	10			
Psychoanaleptics	9			
Psycholeptics	7			
Antibacterials for systemic use	7			
Drugs for obstructive airway diseases	9			
Lipid modifying agents	4			
Agents acting on the renin-angiotensin system	3			
Thyroid therapy	5			
Antihistamines for systemic use	3			
Antithrombotic agents	4			
Nasal preparations	7			
Diuretics	5			
Antianemic preparations	2			
Mineral supplements	3			
Calcium channel blockers	3			
Drugs used in diabetes	6			
Beta blocking agents	1			

Ophthalmologicals	1			
Urologicals	1			
Antidiarrheals, intestinal agents (1)	3			
Antivirals for systemic use	0			
Corticosteroids for systemic use	3			
Drugs for constipation	1			
Anesthetics	0			
Antiemetics and antinauseants	2			
Drugs for functional gastrointestinal disorders	2			
General nutrients	2			
Topical products for joint and muscular pain	2			
Antifungals for dermatological use	1			
Antiobesity preparations, excl. Diet products	1			
Corticosteroids, dermatological preparations	0			
Cough and cold preparations	0			
Other nervous system drugs	1			
Unspecified herbal and traditional medicine	1			
All other therapeutic products	0			
Anti-acne preparations	0			
Other alimentary tract and metabolism products	0			
Throat preparations	1			
Vaccines	0			
Antiepileptics	0			
Antihemorrhagics	1			
Antihypertensives	0			
Antiprotozoals	1			
Antipruritics, incl. antihistamines, anesthetics	1			
Antipsoriatics	1			
Bile and liver therapy	0			
Drugs for treatment of bone diseases	0			
Gynecological antiinfectives and antiseptics	0			
Immunosuppressants	0			
Other respiratory system products	1			
Stomatological preparations	1			
Tonics	0			
Muscle relaxants	2			
Antibiotics,chemotherapeutics (dermatological use)	0			
Antimycotics for systemic use	0			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs (systolic blood pressure) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (systolic blood pressure) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure, pulse rate, temperature, weight, waist circumference, and height, were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	123.2 (± 10.4)	124.2 (± 10.1)	128.9 (± 9.8)	124.6 (± 10.9)
Week 2: Change from baseline (N=44,31,17,52,51)	0.3 (± 12.5)	-0.2 (± 9.0)	-1.5 (± 12.5)	-2.9 (± 9.3)
Week 4: Change from baseline (N=45,31,17,51,48)	1.7 (± 12.4)	0.1 (± 11.9)	-3.1 (± 9.4)	-4.7 (± 10.7)
Week 8: Change from baseline (N=44,31,16,52,46)	0.5 (± 10.8)	0.5 (± 12.5)	-2.1 (± 10.1)	-1.3 (± 10.0)
Week 12: Change from baseline (N=44,30,16,50,45)	-0.6 (± 12.2)	-2.1 (± 10.9)	-5.9 (± 11.3)	-1.1 (± 10.2)
Week 16: Change from baseline (N=43,30,16,51,45)	3.8 (± 13.3)	-0.9 (± 11.7)	-6.4 (± 11.1)	-1.4 (± 10.8)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	124.0 (± 12.9)			
Week 2: Change from baseline (N=44,31,17,52,51)	-0.8 (± 9.2)			
Week 4: Change from baseline (N=45,31,17,51,48)	-1.3 (± 10.8)			
Week 8: Change from baseline (N=44,31,16,52,46)	-3.8 (± 10.5)			
Week 12: Change from baseline (N=44,30,16,50,45)	-1.3 (± 12.8)			
Week 16: Change from baseline (N=43,30,16,51,45)	2.1 (± 9.4)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs (pulse rate) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (pulse rate) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure, pulse rate, temperature, weight, waist circumference, and height, were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: beats/min				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	69.7 (± 7.8)	71.4 (± 10.3)	70.6 (± 8.7)	70.1 (± 10.2)
Week 2: Change from baseline (N=44,31,17,52,51)	-0.1 (± 8.1)	-0.3 (± 7.3)	-0.7 (± 9.9)	-3.1 (± 9.7)
Week 4: Change from baseline (N=45,31,17,51,48)	-0.6 (± 6.9)	0.5 (± 7.6)	-2.8 (± 8.9)	-1.8 (± 6.4)
Week 8: Change from baseline (N=44,31,16,52,46)	0.4 (± 7.7)	-0.5 (± 8.1)	-3.1 (± 9.8)	-2.8 (± 7.9)
Week 12: Change from baseline (N=44,30,16,50,45)	0.1 (± 9.2)	0.3 (± 8.4)	0.9 (± 8.8)	-1.4 (± 8.8)
Week 16: Change from baseline (N=43,30,16,51,45)	3.2 (± 10.6)	3.3 (± 10.5)	0.0 (± 11.3)	-0.7 (± 8.5)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: beats/min				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	69.7 (± 10.2)			



Week 2: Change from baseline (N=44,31,17,52,51)	2.1 (± 9.4)			
Week 4: Change from baseline (N=45,31,17,51,48)	0.9 (± 7.7)			
Week 8: Change from baseline (N=44,31,16,52,46)	0.3 (± 8.1)			
Week 12: Change from baseline (N=44,30,16,50,45)	0.9 (± 7.4)			
Week 16: Change from baseline (N=43,30,16,51,45)	0.3 (± 8.4)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs (temperature) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (temperature) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure, pulse rate, temperature, weight, waist circumference, and height, were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Celsius (C)				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	36.69 (± 0.43)	36.62 (± 0.32)	36.73 (± 0.30)	36.52 (± 0.46)
Week 2: Change from baseline (N=44,31,17,52,51)	-0.09 (± 0.40)	-0.04 (± 0.28)	0.04 (± 0.26)	0.12 (± 0.50)
Week 4: Change from baseline (N=45,31,17,50,48)	-0.15 (± 0.47)	-0.06 (± 0.34)	0.01 (± 0.41)	0.12 (± 0.46)
Week 8: Change from baseline (N=44,31,16, 52,46)	-0.09 (± 0.38)	-0.01 (± 0.35)	0.00 (± 0.31)	0.11 (± 0.49)
Week 12: Change from baseline (N=44,30,16,50,45)	-0.12 (± 0.44)	-0.12 (± 0.31)	-0.03 (± 0.38)	0.04 (± 0.46)
Week 16: Change from baseline (N=43,30,16,51,45)	-0.07 (± 0.50)	-0.03 (± 0.30)	-0.04 (± 0.32)	0.08 (± 0.41)

End point values	160 mg BAY3427080			
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Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Celsius (C)				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	36.68 (± 0.39)			
Week 2: Change from baseline (N=44,31,17,52,51)	-0.01 (± 0.43)			
Week 4: Change from baseline (N=45,31,17,50,48)	-0.06 (± 0.32)			
Week 8: Change from baseline (N=44,31,16, 52,46)	-0.01 (± 0.42)			
Week 12: Change from baseline (N=44,30,16,50,45)	-0.08 (± 0.36)			
Week 16: Change from baseline (N=43,30,16,51,45)	-0.09 (± 0.41)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs (weight) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (weight) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure, pulse rate, temperature, weight, waist circumference, and height, were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Kilogram (Kg)				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	75.85 (± 13.13)	72.65 (± 14.76)	78.14 (± 15.75)	72.36 (± 15.26)
Week 2: Change from baseline (N=44,31,17,52,51)	0.20 (± 1.07)	0.30 (± 1.03)	0.13 (± 1.32)	-0.13 (± 1.19)
Week 4: Change from baseline (N=45,31,17,51,48)	0.23 (± 1.51)	0.08 (± 1.11)	0.12 (± 1.88)	-0.31 (± 1.26)
Week 8: Change from baseline (N=44,31,16,52,46)	0.16 (± 1.98)	0.26 (± 1.59)	-0.11 (± 1.79)	-0.18 (± 1.78)
Week 12: Change from baseline (N=44,30,16,50,45)	-0.02 (± 2.34)	0.58 (± 2.46)	-0.14 (± 2.03)	-0.08 (± 1.93)
Week 16: Change from baseline (N=43,30,16,51,45)	0.17 (± 2.48)	0.39 (± 2.81)	-0.13 (± 2.59)	-0.20 (± 2.13)

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Kilogram (Kg)				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	74.11 (± 15.02)			
Week 2: Change from baseline (N=44,31,17,52,51)	0.04 (± 0.84)			
Week 4: Change from baseline (N=45,31,17,51,48)	0.00 (± 1.35)			
Week 8: Change from baseline (N=44,31,16,52,46)	-0.25 (± 2.32)			
Week 12: Change from baseline (N=44,30,16,50,45)	-0.48 (± 2.62)			
Week 16: Change from baseline (N=43,30,16,51,45)	-0.34 (± 2.82)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs (Body Mass Index ) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (Body Mass Index ) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure, pulse rate, temperature, weight, waist circumference, and height, were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

<b>End point values</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: kg/m2				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	28.59 (± 3.81)	27.69 (± 4.97)	29.81 (± 4.93)	27.26 (± 4.85)
Week 2: Change from baseline (N=44,31,17,52,51)	0.07 (± 0.41)	0.11 (± 0.39)	0.06 (± 0.5)	-0.04 (± 0.45)
Week 4: Change from baseline (N=45,31,17,51,48)	0.07 (± 0.58)	0.02 (± 0.42)	0.06 (± 0.75)	-0.11 (± 0.49)

Week 8: Change from baseline (N=44,31,16,52,46)	0.04 (± 0.75)	0.09 (± 0.59)	-0.04 (± 0.69)	-0.06 (± 0.66)
Week 12: Change from baseline (N=44,30,16,50,45)	-0.03 (± 0.87)	0.21 (± 0.87)	-0.05 (± 0.79)	-0.02 (± 0.73)
Week 16: Change from baseline (N=43,30,16,51,45)	0.04 (± 0.96)	0.13 (± 1.01)	-0.04 (± 1.01)	-0.07 (± 0.79)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: kg/m2				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	27.72 (± 4.74)			
Week 2: Change from baseline (N=44,31,17,52,51)	0.01 (± 0.33)			
Week 4: Change from baseline (N=45,31,17,51,48)	0.00 (± 0.53)			
Week 8: Change from baseline (N=44,31,16,52,46)	-0.09 (± 0.88)			
Week 12: Change from baseline (N=44,30,16,50,45)	-0.18 (± 0.99)			
Week 16: Change from baseline (N=43,30,16,51,45)	-0.13 (± 1.07)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs (waist circumference) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (waist circumference) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure, pulse rate, temperature, weight, waist circumference, and height, were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

From baseline to Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: cm				
arithmetic mean (standard deviation)				
Baseline (N=46,31,17,50,52)	95.47 (± 11.69)	93.61 (± 13.10)	97.59 (± 13.15)	91.12 (± 13.03)
Week 2: Change from baseline (N=43,31,17,49,51)	0.26 (± 3.99)	0.79 (± 3.55)	-0.91 (± 2.15)	0.13 (± 3.72)
Week 4: Change from baseline (N=44,31,17,48,48)	0.17 (± 4.99)	-0.07 (± 4.23)	-1.26 (± 3.00)	0.05 (± 3.84)
Week 8: Change from baseline (N=43,31,16,50,45)	-0.14 (± 4.45)	-0.11 (± 4.30)	0.04 (± 2.77)	-0.76 (± 4.10)
Week 12: Change from baseline (N=43,30,16,48,45)	-1.72 (± 5.25)	-1.16 (± 4.87)	0.60 (± 2.81)	-0.25 (± 3.97)
Week 16: Change from baseline (N=42,30,16, 49,44)	-0.80 (± 5.46)	-0.99 (± 5.18)	4.33 (± 12.90)	0.02 (± 4.58)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: cm				
arithmetic mean (standard deviation)				
Baseline (N=46,31,17,50,52)	92.42 (± 12.36)			
Week 2: Change from baseline (N=43,31,17,49,51)	-0.18 (± 3.90)			
Week 4: Change from baseline (N=44,31,17,48,48)	-0.09 (± 3.97)			
Week 8: Change from baseline (N=43,31,16,50,45)	-0.08 (± 4.71)			
Week 12: Change from baseline (N=43,30,16,48,45)	-0.39 (± 4.42)			
Week 16: Change from baseline (N=42,30,16, 49,44)	-0.24 (± 4.41)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with normal electrocardiogram (ECG) findings at each visit

End point title	Number of subjects with normal electrocardiogram (ECG) findings at each visit
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End point description:

All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. The Investigator commented on all abnormal findings and determined whether they were Normal, Abnormal not clinically significant, Abnormal clinically significant. In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
End point timeframe:	
At Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Baseline (N=47,31,17,52,52)	38	24	11	31
Week 2 (N= 44,31,17,52,51)	33	23	12	34
Week 4 (N=45,31,17,51,48)	32	23	10	28
Week 8 (N=44,31,17,52,46)	29	21	12	30
Week 12 (N=44,30,16,50,45)	30	22	11	31
Week 16 (N=43,30,16,51,45)	27	26	14	31

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Baseline (N=47,31,17,52,52)	34			
Week 2 (N= 44,31,17,52,51)	27			
Week 4 (N=45,31,17,51,48)	31			
Week 8 (N=44,31,17,52,46)	27			
Week 12 (N=44,30,16,50,45)	31			
Week 16 (N=43,30,16,51,45)	28			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs (diastolic blood pressure) at Weeks 2, 4, 8, 12 and 16

End point title	Change from baseline in vital signs (diastolic blood pressure) at Weeks 2, 4, 8, 12 and 16
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End point description:

Vital signs, including systolic and diastolic blood pressure were measured at the time points and recorded in the eCRF. All vital signs were reviewed by the Investigator or delegated physician.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
End point timeframe:	
From baseline to Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	80.1 (± 8.0)	78.7 (± 8.5)	79.9 (± 9.1)	78.1 (± 7.6)
Week 2: Change from baseline (N=44,31,16,52,51)	-0.7 (± 6.6)	-1.1 (± 8.4)	-0.8 (± 8.7)	-3.1 (± 7.6)
Week 4: Change from baseline (N=45,31,17,51,48)	-0.2 (± 7.4)	1.2 (± 7.8)	-2.1 (± 6.5)	-2.8 (± 9.1)
Week 8: Change from baseline (N=44,31,16,52,46)	0.2 (± 6.7)	-0.5 (± 6.8)	-3.6 (± 6.9)	-0.6 (± 8.4)
Week 12: Change from baseline (N=44,30,16,50,45)	-0.5 (± 9.6)	-2.8 (± 9.9)	-2.2 (± 7.1)	-1.8 (± 10.3)
Week 16: Change from baseline (N=43,30,16,51,45)	1.6 (± 7.6)	-1.2 (± 8.3)	-3.8 (± 9.7)	-1.9 (± 9.1)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline (N=47,31,17,52,52)	78.7 (± 10.1)			
Week 2: Change from baseline (N=44,31,16,52,51)	-0.4 (± 7.6)			
Week 4: Change from baseline (N=45,31,17,51,48)	-2.3 (± 8.0)			
Week 8: Change from baseline (N=44,31,16,52,46)	-1.6 (± 7.5)			
Week 12: Change from baseline (N=44,30,16,50,45)	-1.0 (± 9.3)			
Week 16: Change from baseline (N=43,30,16,51,45)	0.6 (± 7.2)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with abnormal not clinically significant ECG findings at each visit

End point title	Number of subjects with abnormal not clinically significant ECG findings at each visit
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End point description:

All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. The Investigator commented on all abnormal findings and determined whether they were Normal, Abnormal

not clinically significant, Abnormal clinically significant.

End point type	Secondary
End point timeframe:	
At Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Baseline (N=47,31,17,52,52)	9	7	6	21
Week 2 (N=44,31,17,52,51)	11	8	5	18
Week 4 (N=45,31,17,51,48)	13	8	6	23
Week 8 (N=44,31,17,52,46)	15	10	5	21
Week 12 (N=44,30,16,50,45)	14	8	5	19
Week 16 (N=43,30,16,51,45)	16	4	2	20

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Baseline (N=47,31,17,52,52)	18			
Week 2 (N=44,31,17,52,51)	24			
Week 4 (N=45,31,17,51,48)	17			
Week 8 (N=44,31,17,52,46)	19			
Week 12 (N=44,30,16,50,45)	14			
Week 16 (N=43,30,16,51,45)	17			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with abnormal clinically significant ECG findings at each visit

End point title	Number of subjects with abnormal clinically significant ECG findings at each visit
End point description:	
All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. The Investigator commented on all abnormal findings and determined whether they were Normal, Abnormal not clinically significant, Abnormal clinically significant. In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.	
End point type	Secondary



End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Baseline (N=47,31,17,52,52)	0	0	0	0
Week 2 (N= 44,31,17,52,51)	0	0	0	0
Week 4 (N=45,31,17,51,48)	0	0	1	0
Week 8 (N=44,31,17,52,46)	0	0	0	1
Week 12 (N=44,30,16,50,45)	0	0	0	0
Week 16 (N=43,30,16,51,45)	0	0	0	0

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Baseline (N=47,31,17,52,52)	0			
Week 2 (N= 44,31,17,52,51)	0			
Week 4 (N=45,31,17,51,48)	0			
Week 8 (N=44,31,17,52,46)	0			
Week 12 (N=44,30,16,50,45)	0			
Week 16 (N=43,30,16,51,45)	0			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (RR)

End point title	Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (RR)
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End point description:

All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. The same model of ECG recorder was used throughout the study for any given subject wherever possible. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. Reports were then filed with the subject's medical record.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

At Weeks 2, 4, 8, 12 and 16

<b>End point values</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	913.5 (± 128.5)	891.4 (± 145.6)	934.3 (± 120.3)	927.8 (± 135.5)
Week 2: Change from baseline (N=44,31,17,52,51)	17.3 (± 84.2)	23.0 (± 101.7)	-12.6 (± 99.7)	27.3 (± 94.7)
Week 4: Change from baseline (N=45,31,17,51,48)	1.6 (± 82.8)	24.8 (± 101.9)	20.5 (± 108.5)	27.3 (± 92.6)
Week 8: Change from baseline (N=44,31,17,52,46)	35.8 (± 108.7)	24.8 (± 104.6)	19.0 (± 128.6)	22.3 (± 109.2)
Week 12: Change from baseline (N=44,30,16,50,45)	25.5 (± 143.4)	18.0 (± 110.9)	-23.3 (± 105.1)	27.2 (± 95.9)
Week 16: Change from baseline (N=43,30,16,51,45)	-22.4 (± 135.5)	2.4 (± 138.5)	-25.4 (± 149.6)	5.9 (± 110.8)

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	935.9 (± 151.2)			
Week 2: Change from baseline (N=44,31,17,52,51)	-2.6 (± 137.7)			
Week 4: Change from baseline (N=45,31,17,51,48)	4.5 (± 108.0)			
Week 8: Change from baseline (N=44,31,17,52,46)	-22.6 (± 90.1)			
Week 12: Change from baseline (N=44,30,16,50,45)	-1.4 (± 107.9)			
Week 16: Change from baseline (N=43,30,16,51,45)	-8.0 (± 110.3)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (PR)

End point title	Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (PR)
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End point description:

All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. The same model of ECG recorder was used throughout the study for any given subject wherever possible. All

ECG reports were reviewed, signed and dated by the Investigator or delegated physician. Reports were then filed with the subject's medical record.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
End point timeframe:	
At Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	162.6 (± 21.8)	167.8 (± 16.5)	162.9 (± 21.7)	157.2 (± 21.7)
Week 2: Change from baseline (N=44,31,17,52,51)	1.2 (± 9.7)	4.6 (± 11.7)	5.2 (± 11.8)	3.0 (± 10.2)
Week 4: Change from baseline (N=45,31,17,51,48)	0.0 (± 11.2)	5.9 (± 12.3)	2.9 (± 12.1)	3.8 (± 17.7)
Week 8: Change from baseline (N=44,31,17,52,46)	1.5 (± 15.1)	3.6 (± 10.4)	-0.1 (± 12.3)	4.3 (± 10.3)
Week 12: Change from baseline (N=44,30,16,50,45)	1.6 (± 11.5)	3.9 (± 11.7)	0.7 (± 16.2)	1.9 (± 11.4)
Week 16: Change from baseline (N=43,30,16,51,45)	0.4 (± 11.3)	2.2 (± 13.3)	2.4 (± 16.0)	2.8 (± 11.1)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	164.2 (± 25.8)			
Week 2: Change from baseline (N=44,31,17,52,51)	-2.2 (± 16.3)			
Week 4: Change from baseline (N=45,31,17,51,48)	1.8 (± 13.8)			
Week 8: Change from baseline (N=44,31,17,52,46)	-1.1 (± 14.5)			
Week 12: Change from baseline (N=44,30,16,50,45)	-1.5 (± 16.9)			
Week 16: Change from baseline (N=43,30,16,51,45)	-0.4 (± 13.3)			

## Statistical analyses

No statistical analyses for this end point

**Secondary: Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (QT)**

End point title	Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (QT)
End point description:	
All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. The same model of ECG recorder was used throughout the study for any given subject wherever possible. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. Reports were then filed with the subject's medical record.	
In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.	
End point type	Secondary
End point timeframe:	
At Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	394.5 (± 31.2)	397.2 (± 28.7)	403.5 (± 26.9)	402.3 (± 40.3)
Week 2: Change from baseline (N=44,31,17,52,51)	3.6 (± 18.0)	0.2 (± 17.8)	1.1 (± 21.7)	-0.9 (± 35.6)
Week 4: Change from baseline (N=45,31,17,51,48)	4.7 (± 18.5)	-0.1 (± 18.5)	4.8 (± 35.2)	0.2 (± 28.1)
Week 8: Change from baseline (N=44,31,17,52,46)	2.0 (± 19.0)	1.5 (± 17.2)	6.5 (± 28.4)	0.5 (± 34.6)
Week 12: Change from baseline (N=44,30,16,50,45)	1.4 (± 25.1)	0.8 (± 21.6)	-8.9 (± 20.6)	-1.1 (± 32.9)
Week 16: Change from baseline (N=43,30,16,51,45)	-1.7 (± 23.3)	-4.7 (± 24.4)	-3.2 (± 27.6)	-4.1 (± 38.1)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	401.2 (± 28.0)			
Week 2: Change from baseline (N=44,31,17,52,51)	-3.2 (± 25.2)			
Week 4: Change from baseline (N=45,31,17,51,48)	0.8 (± 21.5)			
Week 8: Change from baseline (N=44,31,17,52,46)	-4.0 (± 20.3)			
Week 12: Change from baseline (N=44,30,16,50,45)	1.0 (± 19.5)			
Week 16: Change from baseline (N=43,30,16,51,45)	-2.4 (± 25.5)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (QTc)

End point title	Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (QTc)
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End point description:

All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. The same model of ECG recorder was used throughout the study for any given subject wherever possible. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. Reports were then filed with the subject's medical record. QTc: QT corrected interval.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	410.6 (± 20.9)	417.9 (± 21.4)	416.4 (± 14.1)	415.9 (± 29.3)
Week 2: Change from baseline (N=44,31,17,52,51)	1.6 (± 14.3)	-2.4 (± 11.2)	2.9 (± 14.7)	-4.9 (± 28.2)
Week 4: Change from baseline (N=45,31,17,51,48)	5.6 (± 16.1)	-5.4 (± 11.8)	1.7 (± 19.9)	-2.9 (± 24.5)
Week 8: Change from baseline (N=44,31,17,52,46)	-3.9 (± 18.5)	-3.8 (± 12.3)	2.3 (± 10.8)	-2.2 (± 27.5)
Week 12: Change from baseline (N=44,30,16,50,45)	-2.4 (± 20.8)	-3.2 (± 14.9)	-3.1 (± 14.4)	-4.7 (± 31.3)
Week 16: Change from baseline (N=43,30,16,51,45)	2.8 (± 14.9)	-4.8 (± 13.6)	4.3 (± 17.5)	-4.5 (± 31.2)

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	415.2 (± 22.1)			

Week 2: Change from baseline (N=44,31,17,52,51)	-2.1 (± 15.4)			
Week 4: Change from baseline (N=45,31,17,51,48)	0.2 (± 16.3)			
Week 8: Change from baseline (N=44,31,17,52,46)	1.2 (± 14.7)			
Week 12: Change from baseline (N=44,30,16,50,45)	0.5 (± 14.4)			
Week 16: Change from baseline (N=43,30,16,51,45)	-1.6 (± 13.6)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (QTcF)

End point title	Change from baseline at Weeks 2, 4, 8, 12 and 16 in ECG intervals (QTcF)
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End point description:

All ECGs were performed after the subject had rested for 5 minutes in a semi-recumbent position. The same model of ECG recorder was used throughout the study for any given subject wherever possible. All ECG reports were reviewed, signed and dated by the Investigator or delegated physician. Reports were then filed with the subject's medical record. QTcF: QT interval with Fridericia's correction.

In categories the number of subjects analyzed (N) for each week is mentioned for each reporting group respectively.

End point type	Secondary
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End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	407.2 (± 20.6)	413.8 (± 19.9)	413.2 (± 14.3)	413.1 (± 30.7)
Week 2: Change from baseline (N=44,31,17,52,51)	1.2 (± 13.7)	-3.5 (± 10.2)	3.4 (± 13.4)	-4.8 (± 29.5)
Week 4: Change from baseline (N=45,31,17,51,48)	4.8 (± 16.4)	-4.2 (± 11.5)	2.1 (± 23.4)	-3.5 (± 24.7)
Week 8: Change from baseline (N=44,31,17,52,46)	-2.8 (± 15.9)	-2.7 (± 10.9)	4.0 (± 13.2)	-2.6 (± 28.7)
Week 12: Change from baseline (N=44,30,16,50,45)	-1.7 (± 18.5)	-1.9 (± 13.9)	-5.1 (± 13.2)	-5.1 (± 30.8)
Week 16: Change from baseline (N=43,30,16,51,45)	2.6 (± 15.1)	-5.6 (± 14.2)	1.5 (± 14.5)	-4.8 (± 32.7)

End point values	160 mg BAY3427080			
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Subject group type	Reporting group			
Number of subjects analysed	52			
Units: mSec				
arithmetic mean (standard deviation)				
Baseline	411.4 (± 18.6)			
Week 2: Change from baseline (N=44,31,17,52,51)	-2.5 (± 15.7)			
Week 4: Change from baseline (N=45,31,17,51,48)	0.4 (± 15.4)			
Week 8: Change from baseline (N=44,31,17,52,46)	-0.4 (± 16.1)			
Week 12: Change from baseline (N=44,30,16,50,45)	1.1 (± 14.6)			
Week 16: Change from baseline (N=43,30,16,51,45)	-1.3 (± 16.4)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with absolute QTcF values by category at each visit: ≤450, >450 to ≤480, >480 to ≤500, >500 msec

End point title	Number of subjects with absolute QTcF values by category at each visit: ≤450, >450 to ≤480, >480 to ≤500, >500 msec
End point description:	
Absolute QTcF values reported. Number of subjects analyzed at for each reporting group respectively was as follow: Baseline N=47, 31, 17, 52, 52; Week 1 N=44, 31, 17, 52, 52; Week 4 N=45, 31, 17, 51, 48; Week 8 N=44, 31, 17, 52, 46; Week 12 N=44, 30, 16, 50, 45; Week 16 N=43, 30, 16, 51, 45.	
End point type	Secondary
End point timeframe:	
From baseline to Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Baseline: ≤450 msec	46	30	16	51
Baseline: >450 to ≤480 msec	1	1	1	0
Baseline: >480 to ≤500 msec	0	0	0	0
Baseline: >500 msec	0	0	0	1
Week 2: ≤450 msec	44	30	16	52
Week 2: >450 to ≤480 msec	0	1	1	0
Week 2: >480 to ≤500 msec	0	0	0	0
Week 2: >500 msec	0	0	0	0
Week 4: ≤450 msec	44	30	16	51
Week 4: >450 to ≤480 msec	1	1	0	0
Week 4: >480 to ≤500 msec	0	0	0	0
Week 4: >500 msec	0	0	1	0

Week 8: ≤450 msec	44	30	17	52
Week 8: >450 to ≤480 msec	0	1	0	0
Week 8: >480 to ≤500 msec	0	0	0	0
Week 8: >500 msec	0	0	0	0
Week 12: ≤450 msec	44	30	16	50
Week 12: >450 to ≤480 msec	0	0	0	0
Week 12: >480 to ≤500 msec	0	0	0	0
Week 12: >500 msec	0	0	0	0
Week 16: ≤450 msec	42	30	15	51
Week 16: >450 to ≤480 msec	1	0	1	0
Week 16: >480 to ≤500 msec	0	0	0	0
Week 16: >500 msec	0	0	0	0

<b>End point values</b>	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Baseline: ≤450 msec	50			
Baseline: >450 to ≤480 msec	2			
Baseline: >480 to ≤500 msec	0			
Baseline: >500 msec	0			
Week 2: ≤450 msec	50			
Week 2: >450 to ≤480 msec	1			
Week 2: >480 to ≤500 msec	0			
Week 2: >500 msec	0			
Week 4: ≤450 msec	47			
Week 4: >450 to ≤480 msec	1			
Week 4: >480 to ≤500 msec	0			
Week 4: >500 msec	0			
Week 8: ≤450 msec	46			
Week 8: >450 to ≤480 msec	0			
Week 8: >480 to ≤500 msec	0			
Week 8: >500 msec	0			
Week 12: ≤450 msec	45			
Week 12: >450 to ≤480 msec	0			
Week 12: >480 to ≤500 msec	0			
Week 12: >500 msec	0			
Week 16: ≤450 msec	44			
Week 16: >450 to ≤480 msec	1			
Week 16: >480 to ≤500 msec	0			
Week 16: >500 msec	0			

## Statistical analyses

No statistical analyses for this end point



**Secondary: Number of subjects with change from baseline in ECG QTcF values by category at Weeks 2, 4, 8, 12 and 16: ≤0, >0 to ≤30, >30 to ≤60, >60 msec**

End point title	Number of subjects with change from baseline in ECG QTcF values by category at Weeks 2, 4, 8, 12 and 16: ≤0, >0 to ≤30, >30 to ≤60, >60 msec
End point description:	
Increase from Baseline overtime was reported. Number of subjects analyzed at for each reporting group respectively was as follow: Baseline N=47, 31, 17, 52, 52; Week 1 N=44, 31, 17, 52, 52; Week 4 N=45, 31, 17, 51, 48; Week 8 N=44, 31, 17, 52, 46; Week 12 N=44, 30, 16, 50, 45; Week 16 N=43, 30, 16, 51, 45.	
End point type	Secondary
End point timeframe:	
From baseline to Weeks 2, 4, 8, 12 and 16	

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	31	17	52
Units: Subjects				
Week 2: ≤0 msec	19	21	8	27
Week 2: >0 to ≤30 msec	25	10	8	24
Week 2: >30 to ≤60 msec	0	0	1	1
Week 2: >60 msec	0	0	0	0
Week 4: ≤0 msec	20	20	8	27
Week 4: >0 to ≤30 msec	23	11	8	24
Week 4: >30 to ≤60 msec	2	0	0	0
Week 4: >60 msec	0	0	1	0
Week 8: ≤0 msec	24	20	8	25
Week 8: >0 to ≤30 msec	20	11	9	26
Week 8: >30 to ≤60 msec	0	0	0	1
Week 8: >60 msec	0	0	0	0
Week 12: ≤0 msec	24	15	10	29
Week 12: >0 to ≤30 msec	19	15	6	21
Week 12: >30 to ≤60 msec	1	0	0	0
Week 12: >60 msec	0	0	0	0
Week 16: ≤0 msec	18	18	7	26
Week 16: >0 to ≤30 msec	23	12	9	24
Week 16: >30 to ≤60 msec	2	0	0	1
Week 16: >60 msec	0	0	0	0

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Week 2: ≤0 msec	29			
Week 2: >0 to ≤30 msec	22			
Week 2: >30 to ≤60 msec	0			

Week 2: >60 msec	0			
Week 4: <=0 msec	24			
Week 4: >0 to <=30 msec	22			
Week 4: >30 to <=60 msec	2			
Week 4: >60 msec	0			
Week 8: <=0 msec	19			
Week 8: >0 to <=30 msec	26			
Week 8: >30 to <=60 msec	1			
Week 8: >60 msec	0			
Week 12: <=0 msec	22			
Week 12: >0 to <=30 msec	22			
Week 12: >30 to <=60 msec	1			
Week 12: >60 msec	0			
Week 16: <=0 msec	24			
Week 16: >0 to <=30 msec	20			
Week 16: >30 to <=60 msec	1			
Week 16: >60 msec	0			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in the electronic Columbia Suicide Severity Rating Scale (eC-SSRS) at Weeks 4, 12 and 16

End point title	Change from baseline in the electronic Columbia Suicide Severity Rating Scale (eC-SSRS) at Weeks 4, 12 and 16
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End point description:

The Columbia Suicide Severity Rating Scale (C-SSRS) is a rating scale created to evaluate suicidality in adults and children over the age of 12. It rates an individual's degree of suicidal ideation on a scale, ranging from "wish to be dead" to "active suicidal ideation with specific plan and intent." The version used was the eC-SSRS, which is a subject-reported version of the scale. Shifts from baseline versus post-baseline to demonstrate changes in categories (cat) were reported using cat 1 (No Suicidal Ideation or Behaviour), cat 2 (Suicidal Ideation) and cat 3 (Suicidal Behaviour).

End point type	Secondary
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End point timeframe:

Baseline to Weeks 4, 12 and 16

End point values	Placebo	40 mg BAY3427080	80 mg BAY3427080	120 mg BAY3427080
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42 <sup>[6]</sup>	26 <sup>[7]</sup>	16 <sup>[8]</sup>	44 <sup>[9]</sup>
Units: Subjects				
Week 4: shift from cat 1 to cat 1	34	14	13	38
Week 4: shift from cat 1 to cat 2	1	0	0	0
Week 4: shift from cat 1 to cat 3	0	0	0	0
Week 4: shift from cat 2 to cat 1	5	7	2	4
Week 4: shift from cat 2 to cat 2	1	0	0	0
Week 4: shift from cat 2 to cat 3	0	0	0	0
Week 4: shift from cat 3 to cat 1	1	5	1	2

Week 4: shift from cat 3 to cat 2	0	0	0	0
Week 4: shift from cat 3 to cat 3	0	0	0	0
Week 12: shift from cat 1 to cat 1	34	14	12	40
Week 12: shift from cat 1 to cat 2	0	0	0	0
Week 12: shift from cat 1 to cat 3	0	0	0	0
Week 12: shift from cat 2 to cat 1	7	5	3	2
Week 12: shift from cat 2 to cat 2	0	2	0	1
Week 12: shift from cat 2 to cat 3	0	0	0	0
Week 12: shift from cat 3 to cat 1	1	5	1	2
Week 12: shift from cat 3 to cat 2	0	0	0	0
Week 12: shift from cat 3 to cat 3	0	0	0	0
Week 16: shift from cat 1 to cat 1	33	15	12	40
Week 16: shift from cat 1 to cat 2	0	0	0	0
Week 16: shift from cat 1 to cat 3	0	0	0	0
Week 16: shift from cat 2 to cat 1	6	6	3	4
Week 16: shift from cat 2 to cat 2	1	1	0	0
Week 16: shift from cat 2 to cat 3	0	0	0	0
Week 16: shift from cat 3 to cat 1	1	5	1	2
Week 16: shift from cat 3 to cat 2	0	0	0	0
Week 16: shift from cat 3 to cat 3	0	0	0	0

Notes:

[6] - Week 16 N=41

[7] - Week 16 N=27

[8] - Week 12 N=45; Week 16 N=46

[9] - Week 12 N=45; Week 16 N=46

End point values	160 mg BAY3427080			
Subject group type	Reporting group			
Number of subjects analysed	46 <sup>[10]</sup>			
Units: Subjects				
Week 4: shift from cat 1 to cat 1	38			
Week 4: shift from cat 1 to cat 2	0			
Week 4: shift from cat 1 to cat 3	0			
Week 4: shift from cat 2 to cat 1	7			
Week 4: shift from cat 2 to cat 2	0			
Week 4: shift from cat 2 to cat 3	0			
Week 4: shift from cat 3 to cat 1	1			
Week 4: shift from cat 3 to cat 2	0			
Week 4: shift from cat 3 to cat 3	0			
Week 12: shift from cat 1 to cat 1	33			
Week 12: shift from cat 1 to cat 2	0			
Week 12: shift from cat 1 to cat 3	0			
Week 12: shift from cat 2 to cat 1	7			
Week 12: shift from cat 2 to cat 2	0			
Week 12: shift from cat 2 to cat 3	0			
Week 12: shift from cat 3 to cat 1	1			
Week 12: shift from cat 3 to cat 2	0			
Week 12: shift from cat 3 to cat 3	0			
Week 16: shift from cat 1 to cat 1	33			
Week 16: shift from cat 1 to cat 2	0			
Week 16: shift from cat 1 to cat 3	0			

Week 16: shift from cat 2 to cat 1	7			
Week 16: shift from cat 2 to cat 2	0			
Week 16: shift from cat 2 to cat 3	0			
Week 16: shift from cat 3 to cat 1	1			
Week 16: shift from cat 3 to cat 2	0			
Week 16: shift from cat 3 to cat 3	0			

Notes:

[10] - Weeks 12 and 16 N=41

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

On or after first dosing with randomised study treatment up to Week 16

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo

Reporting group title	40 mg BAY3427080
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Reporting group description:

Subjects received 40 mg BAY3427080

Reporting group title	80 mg BAY3427080
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Reporting group description:

Subjects received 80 mg BAY3427080

Reporting group title	120 mg BAY3427080
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Reporting group description:

Subjects received 120 mg BAY3427080

Reporting group title	160 mg BAY3427080
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Reporting group description:

Subjects received 160 mg BAY3427080

Serious adverse events	Placebo	40 mg BAY3427080	80 mg BAY3427080
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 47 (4.26%)	0 / 31 (0.00%)	1 / 17 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 47 (0.00%)	0 / 31 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 31 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Sepsis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 31 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 47 (0.00%)	0 / 31 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 47 (2.13%)	0 / 31 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	120 mg BAY3427080	160 mg BAY3427080	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 52 (1.92%)	1 / 52 (1.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 52 (1.92%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Placebo	40 mg BAY3427080	80 mg BAY3427080
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 47 (38.30%)	13 / 31 (41.94%)	14 / 17 (82.35%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 47 (0.00%)	3 / 31 (9.68%)	1 / 17 (5.88%)
occurrences (all)	0	3	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 31 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	1 / 47 (2.13%)	0 / 31 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 47 (4.26%)	0 / 31 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 47 (0.00%)	2 / 31 (6.45%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Depressed mood			

subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Insomnia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	1 / 31 (3.23%) 1	1 / 17 (5.88%) 2
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Liver function test increased subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 31 (6.45%) 2	0 / 17 (0.00%) 0
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	0 / 17 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	6 / 47 (12.77%) 8	3 / 31 (9.68%) 3	2 / 17 (11.76%) 2
Somnolence			



subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 2	3 / 31 (9.68%) 3	1 / 17 (5.88%) 1
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Diarrhoea subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	2 / 31 (6.45%) 2	2 / 17 (11.76%) 2
Flatulence subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Nausea subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	2 / 31 (6.45%) 4	2 / 17 (11.76%) 2
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	1 / 17 (5.88%) 2
Musculoskeletal and connective tissue disorders			
Joint swelling subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 31 (0.00%) 0	1 / 17 (5.88%) 1
Infections and infestations			
Herpes zoster subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 31 (0.00%) 0	2 / 17 (11.76%) 2
Nasopharyngitis			

subjects affected / exposed	4 / 47 (8.51%)	1 / 31 (3.23%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	2 / 31 (6.45%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 31 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Viral sinusitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 31 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

<b>Non-serious adverse events</b>	120 mg BAY3427080	160 mg BAY3427080	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 52 (44.23%)	23 / 52 (44.23%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 52 (1.92%)	4 / 52 (7.69%)	
occurrences (all)	1	4	
Non-cardiac chest pain			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	1 / 52 (1.92%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 52 (1.92%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 52 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Psychiatric disorders			

Depressed mood subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	0 / 52 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 52 (1.92%) 1	
Investigations			
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 52 (0.00%) 0	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3	1 / 52 (1.92%) 1	
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 52 (0.00%) 0	
Liver function test increased subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 52 (0.00%) 0	
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	1 / 52 (1.92%) 1	
Cardiac disorders			
Bradycardia subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 52 (0.00%) 0	
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 4	3 / 52 (5.77%) 3	
Headache subjects affected / exposed occurrences (all)	6 / 52 (11.54%) 7	4 / 52 (7.69%) 6	
Somnolence			

subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	6 / 52 (11.54%) 6	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 52 (1.92%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	3 / 52 (5.77%)	3 / 52 (5.77%)	
occurrences (all)	3	3	
Flatulence			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	1 / 52 (1.92%)	2 / 52 (3.85%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 52 (1.92%)	1 / 52 (1.92%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences (all)	0	0	
Nephrolithiasis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			

subjects affected / exposed	3 / 52 (5.77%)	0 / 52 (0.00%)	
occurrences (all)	3	0	
Urinary tract infection			
subjects affected / exposed	2 / 52 (3.85%)	2 / 52 (3.85%)	
occurrences (all)	2	2	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 52 (3.85%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Viral sinusitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	
occurrences (all)	0	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 February 2019	<p>In addition to minor typographical and formatting corrections, the following changes were made:</p> <ul style="list-style-type: none"><li>- Clinical Chemistry was added to Week 8 visit.</li><li>- A footnote was added to Inclusion Criterion #3 to provide further clarity and guidance on the definition of post-menopausal status.</li><li>- Haemoglobin A1c was added to the list of clinical chemistry parameters.</li><li>- The CRO's name was updated from Pharm Olam International to Pharm Olam.</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The secondary endpoint "change from baseline in clinical laboratory assessments" will be reported during the next update of the record.

Notes: