Clinical trial results:
A double-blind, randomized, placebo-controlled multicenter study to investigate efficacy and safety of elinzanetant for the treatment of vasomotor symptoms over 52 weeks in postmenopausal women

Summary

EudraCT number	2021-000059-38
Trial protocol	BE ES FI DK BG PL
Global end of trial date	12 February 2024

Results information

Result version number	v1 (current)
This version publication date	13 February 2025
First version publication date	13 February 2025

Trial information

Trial identification

Sponsor protocol code	BAY3427080/21810

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05030584
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, 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	12 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of elinzanetant for the treatment of VMS associated with the menopause

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects (or their legally authorized representative according to local legislation). Participating subjects (or their legally authorized representative according to local legislation) signed informed consent form and could 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	27 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 44
Country: Number of subjects enrolled	Bulgaria: 70
Country: Number of subjects enrolled	Canada: 32
Country: Number of subjects enrolled	Denmark: 24
Country: Number of subjects enrolled	Finland: 32
Country: Number of subjects enrolled	Poland: 91
Country: Number of subjects enrolled	Spain: 50
Country: Number of subjects enrolled	United Kingdom: 40
Country: Number of subjects enrolled	United States: 245
Worldwide total number of subjects	628
EEA total number of subjects	311

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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	628
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 75 study centers in North America and in several countries in Europe, between 27-Aug-2021 (first participant first visit) and 12-Feb-2024 (last participant last visit).

Pre-assignment

Screening details:

A total of 1524 patients were screened, of whom 628 were randomized.

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
Arm title	Elinzanetant (BAY3427080)

Arm description:

Subjects received 120 mg elinzanetant orally once daily.

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

Dosage and administration details:

120 mg elinzanetant orally once daily.

Arm title	Placebo

Arm description:

Subjects received matching placebo orally once daily.

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:

Matching placebo orally once daily.

Number of subjects in period 1	Elinzanetant (BAY3427080)	Placebo
Started	313	315
Received treatment	312	315
Completed	222	231
Not completed	91	84
Physician decision	1	4
Consent withdrawn by subject	21	28
Randomized by Mistake	-	2
Non-Compliance with Study Drug	2	3
Adverse event, non-fatal	17	2
Technical Problems	-	1
non specified	4	3
Lost to follow-up	5	2
Completed post-treatment/FU visits	41	31
Lack of efficacy	-	6
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Elinzanetant (BAY3427080)
Reporting group description:	
Subjects received 120 mg elinzanetant orally once daily.	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo orally once daily.	

Reporting group values	Elinzanetant (BAY3427080)	Placebo	Total
Number of subjects	313	315	628
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	54.6	54.9	
standard deviation	± 4.7	± 5.0	-
Gender Categorical Units: Subjects			
Female	313	315	628
Male	0	0	0
Race Units: Subjects			
Asian	2	2	4
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	51	44	95
White	240	253	493
More than one race	0	1	1
Unknown or Not Reported	19	15	34
Ethnicity Units: Subjects			
Hispanic or Latino	34	34	68
Not Hispanic or Latino	266	273	539
Unknown or Not Reported	13	8	21

End points

End points reporting groups

Reporting group title	Elinzanetant (BAY3427080)
Reporting group description: Subjects received 120 mg elinzanetant orally once daily.	
Reporting group title	Placebo
Reporting group description: Subjects received matching placebo orally once daily.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: All randomized subjects.	
Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects who received at least one dose of study intervention.	

Primary: Mean change in frequency of moderate to severe hot flashes (HFs) from baseline to Week 12 (assessed by hot flash daily diary [HFDD])

End point title	Mean change in frequency of moderate to severe hot flashes (HFs) from baseline to Week 12 (assessed by hot flash daily diary [HFDD])

End point description:

The HFDD items assess the number of mild, moderate, and severe HF experienced during the day and during the night. In addition, the number of awakenings during the night and disturbance of sleep due to HF will be documented in the morning diary. Mild HF are defined as a "sensation of heat without sweating", moderate HF are defined as a "sensation of heat with sweating, but able to continue activity", and severe HF are defined as a "sensation of heat with sweating, causing cessation (stopping) of activity". The frequency of moderate to severe HF for each week during the treatment period was calculated using the available data during that particular week. Specifically, for Week 12, Day 78-84 were used (Day 1 corresponds to start of treatment).

End point type	Primary

End point timeframe:

Baseline to Week 12

End point values	Elinzanetant (BAY3427080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[1]	315[2]		
Units: Number of HF per day				
arithmetic mean (standard deviation)				
Baseline (n=312,315)	6.71 (± 7.15)	6.81 (± 6.15)		
Change from Baseline (n=258,278)	-5.40 (± 7.29)	-3.50 (± 4.96)		

Notes:

[1] - FAS

[2] - FAS

Statistical analyses

Statistical analysis title	MMRM analysis
Statistical analysis description:	
For category "Change from baseline". The number of subjects in the statistical analysis is 555.	
Comparison groups	Elinzanetant (BAY3427080) v Placebo
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Mixed model repeated measures (MMRM)
Parameter estimate	Difference in LS-means
Point estimate	-1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	-1.05

Notes:

[3] - The type I error rate was controlled at a one-sided α=0.025 level.

Secondary: Mean change in patient-reported outcomes measurement information system sleep disturbance short form 8b (PROMIS SD SF 8b) total T-score from baseline over time

End point title	Mean change in patient-reported outcomes measurement information system sleep disturbance short form 8b (PROMIS SD SF 8b) total T-score from baseline over time

End point description:

The PROMIS SD SF 8b includes 8 items assessing sleep disturbance over the past 7 days. Items assess sleep quality, sleep depth and restoration associated with sleep, perceived difficulties with getting to sleep or staying asleep and perceptions of the adequacy of and satisfaction with sleep. Participants respond to the items on a 5-point scale from not at all, never or very poor to very much, always or very good. Four of the items are scored reversely. Total scores range from 8 to 40, with higher scores indicating greater severity of sleep disturbance. The total raw scores were converted to total T-scores for analysis of this endpoint (range 28.9–76.5).

End point type	Secondary

End point timeframe:

Baseline to Week 56

End point values	Elinzanetant (BAY3427080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	315		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=270,274)	57.35 (± 6.66)	57.96 (± 7.63)		
Change from baseline to Week 1 (n=265,270)	-5.19 (± 7.17)	-1.60 (± 5.39)		
Change from baseline to Week 2 (n=262,265)	-6.78 (± 7.96)	-2.89 (± 6.78)		
Change from baseline to Week 3 (n=258,265)	-7.67 (± 8.24)	-3.34 (± 6.88)		
Change from baseline to Week 4 (n=249,263)	-7.70 (± 8.27)	-3.81 (± 6.98)		

Change from baseline to Week 8 (n=241,253)	-7.98 (± 8.58)	-4.36 (± 7.64)		
Change from baseline to Week 12 (n=228,246)	-7.97 (± 8.04)	-5.26 (± 8.02)		
Change from baseline to Week 18 (n=188,192)	-8.83 (± 9.05)	-5.77 (± 7.82)		
Change from baseline to Week 24 (n=178,195)	-9.77 (± 9.00)	-5.85 (± 7.79)		
Change from baseline to Week 36 (n=186,190)	-9.20 (± 8.74)	-5.88 (± 8.38)		
Change from baseline to Week 52 (n=151,159)	-9.36 (± 8.41)	-5.73 (± 7.91)		
Change at Week 56 (Follow-up) (n=184,177)	-5.83 (± 8.71)	-5.38 (± 7.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in menopause specific quality of life scale (MENQOL) total score from baseline over time

End point title	Mean change in menopause specific quality of life scale (MENQOL) total score from baseline over time

End point description:

The MENQOL questionnaire is comprised of 29 items assessing the presence of menopausal symptoms and the impact of menopause on health-related quality of life over the past week. The items assess four domains of symptoms and functioning: Vasomotor functioning, psychosocial functioning, physical functioning, and sexual functioning. For each item, the participant indicates if they have experienced the symptom (yes/no). If they select yes, they rate how bothered they were by the symptom using a six-point verbal descriptor scale, with response options ranging from 0 'not at all bothered' to 6 'extremely bothered'. Based on the individual responses, item scores, domain scores, and a total MENQOL score are calculated. Each score ranges from 1-8, higher scores indicate greater bother.

End point type	Secondary

End point timeframe:

Baseline to Week 56

End point values	Elinzanetant (BAY3427080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	315		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=262,264)	4.10 (± 1.21)	4.41 (± 1.37)		
Change from baseline to Week 4 (n=235,250)	-0.94 (± 1.22)	-0.67 (± 1.21)		
Change from baseline to Week 8 (n=233,243)	-1.07 (± 1.24)	-0.86 (± 1.18)		
Change from baseline to Week 12 (n=220,235)	-1.10 (± 1.25)	-0.95 (± 1.32)		
Change from baseline to Week 18 (n=183,185)	-1.30 (± 1.32)	-1.11 (± 1.40)		
Change from baseline to Week 24 (n=173,185)	-1.25 (± 1.17)	-1.15 (± 1.37)		

Change from baseline to Week 36 (n=179,182)	-1.18 (± 1.21)	-1.02 (± 1.42)		
Change from baseline to Week 52 (n=147,154)	-1.30 (± 1.33)	-1.11 (± 1.35)		
Change at Week 56 (Follow-up) (n=178,172)	-0.82 (± 1.25)	-1.04 (± 1.59)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events tables: up to 14 days from the last drug intake.
All-cause mortality table: after signing informed consent up to the last contact per participant, up to 56 weeks.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Elinzanetant (BAY3427080)

Reporting group description:

Subjects received 120 mg elinzanetant orally once daily.

Reporting group title	Placebo

Reporting group description:

Subjects received matching placebo orally once daily.

Serious adverse events	Elinzanetant (BAY3427080)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 313 (4.15%)	6 / 314 (1.91%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Concussion			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 313 (0.00%)	1 / 314 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Encephalitis toxic			
subjects affected / exposed	0 / 313 (0.00%)	1 / 314 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparaesthesia			
subjects affected / exposed	0 / 313 (0.00%)	1 / 314 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 313 (0.00%)	1 / 314 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 313 (0.32%)	1 / 314 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Epiglottitis			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bite			
subjects affected / exposed	0 / 313 (0.00%)	1 / 314 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis meningococcal			
subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fusobacterium infection			

subjects affected / exposed	1 / 313 (0.32%)	0 / 314 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Elinzanetant (BAY3427080)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 313 (27.16%)	73 / 314 (23.25%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	16 / 313 (5.11%)	4 / 314 (1.27%)	
occurrences (all)	18	4	
Headache			
subjects affected / exposed	30 / 313 (9.58%)	22 / 314 (7.01%)	
occurrences (all)	51	51	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	21 / 313 (6.71%)	9 / 314 (2.87%)	
occurrences (all)	23	9	
Infections and infestations			
COVID-19			
subjects affected / exposed	22 / 313 (7.03%)	32 / 314 (10.19%)	
occurrences (all)	22	32	
Nasopharyngitis			
subjects affected / exposed	15 / 313 (4.79%)	21 / 314 (6.69%)	
occurrences (all)	16	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2022	1. Exclusion criteria were modified. 2. Instructions regarding drugs that are sensitive substrates of OATP1B1/1B3, P-gp or BCRP during co-administration of elinzanetant were updated to allow administration of BCRP and/or OATP1B1/1B3 together with elinzanetant without restrictions. 3. Discontinuation of study intervention and Participant discontinuation/withdrawal from the study sections were updated. 4. Mammogram should be done either prior to COVID-vaccinations, or it should be delayed for a certain period after a vaccination, according to local guidelines. 5. Adverse events of special interest and Close observation of participants with liver function test findings sections were updated. 6. The primary endpoints will be analyzed using a mixed model with repeated measures (MMRM) on the change from baseline scores at different Weeks including also Week 8. 7. Liver safety - related monitoring and discontinuation criteria was updated. 8. Appendix 6: Prohibited concomitant medications was updated.
22 June 2022	1. Demography and baseline characteristics were updated to include educational level, and gynecological and reproductive history including numbers of pregnancy and birth. 2. Inclusion criterion 6: A new sub-bullet was added: HPV testing in participants with "absence of endocervical/transformation zone component" will be used as an adjunctive test automatically. Participants can be included if they are negative for high-risk HPV strains. 3. Exclusion Criteria: Re-test is allowed once in case of an abnormal INR value. 4. All vaginal hormonal products are prohibited from 4 weeks prior to Baseline, and not only those with systemic exposure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported