



Clinical trial results:

A Phase 2, Randomized, Double-blinded, Placebo-controlled, 5 Parallel-group Study of

BMS-986166 or Branebrutinib for the Treatment of Patients with Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2020-004767-77
Trial protocol	ES DE PL
Global end of trial date	22 August 2022

Results information

Result version number	v1 (current)
This version publication date	07 September 2023
First version publication date	07 September 2023

Trial information

Trial identification

Sponsor protocol code	IM018-005
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05014438
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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 December 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of BMS-986166 and of branebrutinib, each versus placebo at Week 16 in patients with moderate-to-severe AD.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 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	Australia: 1
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	17
EEA total number of subjects	9

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)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

17 participants randomized and treated

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description:

Placebo

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

Dosage and administration details:

POQD

Arm title	Treatment 1
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Arm description:

BMS-986166 0.25mg POQD

Arm type	Experimental
Investigational medicinal product name	BMS-986166
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.25mg/0.25mg POQD

Arm title	Treatment 2
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Arm description:

BMS-986166 0.5mg POQD

Arm type	Experimental
Investigational medicinal product name	BMS-986166
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.25mg/0.50mg POQD

Arm title	Treatment 3
Arm description: BMS-986166 0.75mg POQD	
Arm type	Experimental
Investigational medicinal product name	BMS-986166
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 0.25mg/0.75mg POQD	
Arm title	Treatment 4
Arm description: Branebrutinib 9mg POQD	
Arm type	Experimental
Investigational medicinal product name	Branebrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 3mg/9mg POQD	

Number of subjects in period 1	Placebo	Treatment 1	Treatment 2
Started	4	3	4
Completed	3	3	3
Not completed	1	0	1
Discontinued Study	1	-	1

Number of subjects in period 1	Treatment 3	Treatment 4
Started	3	3
Completed	1	3
Not completed	2	0
Discontinued Study	2	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Treatment 1
Reporting group description: BMS-986166 0.25mg POQD	
Reporting group title	Treatment 2
Reporting group description: BMS-986166 0.5mg POQD	
Reporting group title	Treatment 3
Reporting group description: BMS-986166 0.75mg POQD	
Reporting group title	Treatment 4
Reporting group description: Branebrutinib 9mg POQD	

Reporting group values	Placebo	Treatment 1	Treatment 2
Number of subjects	4	3	4
Age categorical Units: Subjects			
Adults (18-64 years)	4	3	4
Age Continuous Units: Years			
arithmetic mean	30.5	36.0	29.5
standard deviation	± 11.3	± 6.2	± 14.6
Sex: Female, Male Units:			
Female	3	1	3
Male	1	2	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	3	3	2
More than one race	0	0	0
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	0
Not Hispanic or Latino	2	3	3
Unknown or Not Reported	0	0	1

Reporting group values	Treatment 3	Treatment 4	Total
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Number of subjects	3	3	17
Age categorical			
Units: Subjects			
Adults (18-64 years)	3	3	17
Age Continuous			
Units: Years			
arithmetic mean	46.7	36.7	
standard deviation	± 8.3	± 17.8	-
Sex: Female, Male			
Units:			
Female	2	2	11
Male	1	1	6
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	3	3	14
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	1	4
Not Hispanic or Latino	2	2	12
Unknown or Not Reported	0	0	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Treatment 1
Reporting group description: BMS-986166 0.25mg POQD	
Reporting group title	Treatment 2
Reporting group description: BMS-986166 0.5mg POQD	
Reporting group title	Treatment 3
Reporting group description: BMS-986166 0.75mg POQD	
Reporting group title	Treatment 4
Reporting group description: Branebrutinib 9mg POQD	

Primary: Mean Percentage change from baseline in EASI Score at week 16

End point title	Mean Percentage change from baseline in EASI Score at week 16 ^[1]
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End point description:

The Eczema Area and Severity Index (EASI) is a validated, composite scoring system assessed by the investigator based on the extent of each of the 4 body regions (head and neck, upper limbs, lower limbs, and trunk) affected with AD and the intensity of each of 4 key signs of AD (erythema, induration/papulation, excoriation, and lichenification) and is based on a 4-point scale of 0 (absent), 1 (mild), 2 (moderate), and 3 (severe). For each of the 4 body regions, the mean intensity of inflamed lesions for each of the 4 signs is recorded. Xerosis, scaling, urticaria, or post-inflammatory pigmentation changes are not included. The total EASI score ranges from 0 to 72.

The lower the score the better.

Here "99999" means NA

End point type	Primary
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End point timeframe:

From baseline to 16 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis done for this endpoint

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0 ^[2]	0 ^[3]	0 ^[4]
Units: Percentage				
arithmetic mean (standard deviation)	-83.1 (± 99999)	()	()	()

Notes:

[2] - No participants analyzed

[3] - No participants analyzed

[4] - No participants analyzed

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Percentage				
arithmetic mean (standard deviation)	-92.3 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants exhibiting a Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) score of 0 (cleared) or 1 (almost cleared) AND a ≥ 2 point reduction from baseline at Week 16

End point title	Percentage of participants exhibiting a Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) score of 0 (cleared) or 1 (almost cleared) AND a ≥ 2 point reduction from baseline at Week 16
End point description:	
The vIGA-AD is a static 5-point assessment intended to assess the global severities of key acute clinical signs of AD, including erythema, induration/papulation, and oozing/crusting (lichenification excluded).	
The rating of cleared (0), almost cleared (1), mild (2), moderate (3), and severe (4) will be assessed.	
End point type	Secondary
End point timeframe:	
From baseline to 16 weeks	

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Percentage of participants				
number (confidence interval 95%)	0 (0.0 to 60.2)	0 (0.0 to 70.8)	0 (0.0 to 60.2)	0 (0.0 to 70.8)

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of participants				
number (confidence interval 95%)	0 (0.0 to 70.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants exhibiting a $\geq 50\%$ (EASI-50) reduction from baseline in EASI score at Week 16

End point title	Percentage of participants exhibiting a $\geq 50\%$ (EASI-50) reduction from baseline in EASI score at Week 16
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End point description:

The Eczema Area and Severity Index (EASI) is a validated, composite scoring system assessed by the investigator based on the extent of each of the 4 body regions (head and neck, upper limbs, lower limbs, and trunk) affected with AD and the intensity of each of 4 key signs of AD (erythema, induration/papulation, excoriation, and lichenification) and is based on a 4-point scale of 0 (absent), 1 (mild), 2 (moderate), and 3 (severe). For each of the 4 body regions, the mean intensity of inflamed lesions for each of the 4 signs is recorded. Xerosis, scaling, urticaria, or post-inflammatory pigmentation changes are not included. The total EASI score ranges from 0 to 72.

The lower the score the better.

End point type	Secondary
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End point timeframe:

From baseline to 16 weeks

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Percentage of participants				
number (confidence interval 95%)	25 (0.6 to 80.6)	0 (0.0 to 70.8)	0 (0.0 to 60.2)	0 (0.0 to 70.8)

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of participants				
number (confidence interval 95%)	33.3 (0.8 to 90.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants exhibiting a ≥ 4 -point improvement from baseline in Pruritus NRS at Week 16

End point title	Percentage of participants exhibiting a ≥ 4 -point improvement from baseline in Pruritus NRS at Week 16
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End point description:

Participants will complete a daily diary recording the intensity of their pruritus and the average quality of sleep they experienced during the preceding 24 hours. The intensity of pruritus will be assessed using a validated 11-point NRS, ranging from 0 ("no itching") to 10 ("the worst itching imaginable"). The quality

of sleep will be assessed using a validated 11-point NRS ranging from 0 ("the best possible sleep") to 10 ("the worst possible sleep").

The lower the score the better.

End point type	Secondary
End point timeframe:	
From baseline to 16 weeks	

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	2	2
Units: Percentage of participants				
number (confidence interval 95%)	25.0 (0.6 to 80.6)	0 (0.0 to 70.8)	0 (0.0 to 84.2)	50 (1.3 to 98.7)

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Percentage of participants				
number (confidence interval 95%)	50 (1.3 to 98.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage change from baseline in Pruritus NRS score at Week 16

End point title	Mean Percentage change from baseline in Pruritus NRS score at Week 16
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End point description:

Participants will complete a daily diary recording the intensity of their pruritus and the average quality of sleep they experienced during the preceding 24 hours. The intensity of pruritus will be assessed using a validated 11-point NRS, ranging from 0 ("no itching") to 10 ("the worst itching imaginable"). The quality of sleep will be assessed using a validated 11-point NRS ranging from 0 ("the best possible sleep") to 10 ("the worst possible sleep").

The lower the score the better.

Here "99999" means NA

End point type	Secondary
End point timeframe:	
From baseline to 16 weeks	

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0 ^[5]	0 ^[6]	1
Units: Percentage				
arithmetic mean (standard deviation)	-89.6 (± 99999)	()	()	-100 (± 99999)

Notes:

[5] - No participants analyzed

[6] - No participants analyzed

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Percentage				
arithmetic mean (standard deviation)	-86.8 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in percentage of affected BSA at Week 16

End point title	Mean change from baseline in percentage of affected BSA at Week 16
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End point description:

A widely used method of measuring Body Surface Area (BSA) involvement by AD, is the rule of nines in which for each section of the body (the possible highest score for each region is: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], genitals [1%]) and will be reported as a percentage of all major body sections combined.

Here "99999" means NA

End point type	Secondary
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End point timeframe:

From baseline to 16 weeks

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0 ^[7]	0 ^[8]	0 ^[9]
Units: Percentage				
arithmetic mean (standard deviation)	-17.00 (± 99999)	()	()	()

Notes:

[7] - No participants analyzed

[8] - No participants analyzed

[9] - No participants analyzed

End point values	Treatment 4			
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Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Percentage				
arithmetic mean (standard deviation)	-12.10 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with mild moderate or severe AEs

End point title	Number of participants with mild moderate or severe AEs
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End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation participant administered study treatment that does not necessarily have a causal relationship with this treatment.

Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities.

Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities.

Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event, and both AEs and SAEs can be assessed as severe.

End point type	Secondary
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End point timeframe:

From initial treatment to 30 days post discontinuation, approximately 29 weeks

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants				
Mild	1	2	1	1
Moderate	1	3	1	1
Severe	0	0	0	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
Mild	1			
Moderate	0			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with mild moderate or severe SAEs

End point title	Number of participants with mild moderate or severe SAEs
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End point description:

A Serious Adverse Event (SAE) is defined as any untoward medical occurrence that, at any dose:

- Results in death
- is life threatening
- Requires inpatient hospitalization or causes prolongation of existing hospitalization
- Results in persistent or significant disability
- Is a congenital anomaly/birth defect.
- Is an important medical event

End point type	Secondary
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End point timeframe:

From initial treatment to 30 days post discontinuation, approximately 29 weeks

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants				
Mild	0	0	0	0
Moderate	0	1	0	0
Severe	0	0	0	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
Mild	0			
Moderate	0			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically relevant ECG abnormalities

End point title	Number of participants with clinically relevant ECG abnormalities
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End point description:

12 Lead Electrocardiogram (ECG).

The participant will remain supine for 5 to 10 minutes prior to the ECG and must have lab work done after the tracing so that the ECG results remain as accurate as possible.

End point type	Secondary
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End point timeframe:

Week 24 after initial treatment

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants	0	0	0	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically relevant OCT abnormalities

End point title	Number of participants with clinically relevant OCT abnormalities
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End point description:

Optical coherence tomography (OCT) is a non-invasive imaging test. It uses light waves to take cross-section pictures of your retina. Diagnosis is made by an ophthalmologist.

End point type	Secondary
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End point timeframe:

Week 24 after initial treatment

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants	0	0	1	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically relevant PFT abnormalities

End point title	Number of participants with clinically relevant PFT abnormalities
End point description: Pulmonary function tests (PFT) include: forced expiratory volume (FEV1), percent predicted FEV1, forced vital capacity (FVC), percent predicted FVC, and Diffusion capacity of carbon monoxide (DLCO).	
End point type	Secondary
End point timeframe: Week 24 after initial treatment	

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants	0	0	0	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically meaningful changes in vital signs

End point title	Number of participants with clinically meaningful changes in vital signs
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End point description:

The following vital signs will be assessed: systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate and body temperature.

End point type	Secondary
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End point timeframe:

Week 24 after initial treatment

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants				
Respiratory Rate	2	1	2	3
Heart Rate	0	0	0	0
Diastolic Blood Pressure	0	0	0	0
Systolic Blood Pressure	0	0	0	0
Body Temperature	0	0	0	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
Respiratory Rate	3			
Heart Rate	0			
Diastolic Blood Pressure	0			
Systolic Blood Pressure	0			
Body Temperature	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically relevant changes in LFTs

End point title	Number of participants with clinically relevant changes in LFTs
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End point description:

Liver Function Tests (LFTs) will include the following measurements:

- ALT OR AST > 3 X ULN
- ALT OR AST > 5 X ULN
- ALT OR AST > 8 X ULN
- TOTAL BILIRUBIN > 2 X ULN
- ALT OR AST > 3 X ULN AND (TOTAL BILIRUBIN > 2 X ULN OR INR >1.5) (labeled as "Assessment 5")
- ALT OR AST > 5 X ULN WITH CONFIRMATION, WITHIN 2 WEEKS (labeled as "Assessment 6")

AST = aspartate aminotransferase

ALT = alanine aminotransferase

ULN = Upper limit number

INR = International Normalized Ratio

End point type	Secondary
End point timeframe:	
Week 24 after initial treatment	

End point values	Placebo	Treatment 1	Treatment 2	Treatment 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	3
Units: Participants				
ALT OR AST > 3 X ULN	0	0	0	0
ALT OR AST > 5 X ULN	0	0	0	0
ALT OR AST > 8 X ULN	0	0	0	0
TOTAL BILIRUBIN > 2 X ULN	0	0	0	0
Assessment 5	0	0	0	0
Assessment 6	0	0	0	0

End point values	Treatment 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
ALT OR AST > 3 X ULN	0			
ALT OR AST > 5 X ULN	0			
ALT OR AST > 8 X ULN	0			
TOTAL BILIRUBIN > 2 X ULN	0			
Assessment 5	0			
Assessment 6	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events: (From first dose to last dose + 8 weeks follow up):
Approximately 24 Weeks

All-Cause mortality (From randomization to end of study): Approximately 29 Weeks

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo

Reporting group title	Treatment 1
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Reporting group description:

BMS-986166 0.25mg POQD

Reporting group title	Treatment 2
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Reporting group description:

BMS-986166 0.5mg POQD

Reporting group title	Treatment 3
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Reporting group description:

BMS-986166 0.75mg POQD

Reporting group title	Treatment 4
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Reporting group description:

Branebrutinib 9mg POQD

Serious adverse events	Placebo	Treatment 1	Treatment 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment 3	Treatment 4	
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Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 %

Non-serious adverse events	Placebo	Treatment 1	Treatment 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	3 / 3 (100.00%)	2 / 4 (50.00%)
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Nodule			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Macular degeneration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all) Skin mass subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 3 (0.00%) 0 1 / 3 (33.33%) 1	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Infections and infestations Furuncle subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Skin bacterial infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1	0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0
Metabolism and nutrition disorders Diabetes mellitus inadequate control subjects affected / exposed occurrences (all) Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0

Non-serious adverse events	Treatment 3	Treatment 4	
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Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
General disorders and administration site conditions Nodule subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	
Eye disorders Macular degeneration subjects affected / exposed occurrences (all) Visual impairment subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all) Skin mass subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	
Psychiatric disorders			

Depressed mood subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
Infections and infestations			
Furuncle subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
Skin bacterial infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	
Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2021	The purpose of this amendment is to incorporate comments from the United States Food and Drug Administration (FDA) and to provide guidance on how to manage the increasing availability of coronavirus disease 2019 (COVID-19) vaccines and their impact on screening and the conduct of the study. This amendment also provides updated branebrutinib clinical pharmacology drug-drug interaction (DDI) data. The EudraCT and UTN regulatory agency identifier numbers were also added to the title page.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported