Clinical trial results:
A Phase 2 Study to Evaluate the Efficacy and Safety of LY3462817 in Participants with Moderately to Severely Active Rheumatoid Arthritis

Summary

EudraCT number	2020-002673-10
Trial protocol	CZ HU PL
Global end of trial date	29 June 2022

Results information

Result version number	v2 (current)
This version publication date	12 July 2023
First version publication date	22 January 2023
Version creation reason	• New data added to full data set Final data to be posted

Trial information

Trial identification

Sponsor protocol code	J1A-MC-KDAD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04634253
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17424

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	29 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The reason for this study is to see if the study drug LY3462817 is safe and effective in participants with moderately to severely active rheumatoid arthritis (RA).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2021
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	Hungary: 28
Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Mexico: 30
Worldwide total number of subjects	98
EEA total number of subjects	50

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)	84

From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No Text Available

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received (0.9% sodium chloride solution) Placebo administered Intravenously.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.9% sodium chloride solution was administered as an IV infusion.

Arm title	LY3462817 300 mg

Arm description:

Participants received 300 milligrams (mg) of LY3462817 administered Intravenously.

Arm type	Experimental
Investigational medicinal product name	LY3462817
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

300 mg of LY3462817 administered as an IV infusion in 50 mg/mL in a 3-mL vial.

Arm title	LY3462817 700 mg

Arm description:

Participants received 700 mg of LY3462817 administered Intravenously.

Arm type	Experimental
Investigational medicinal product name	LY3462817
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

700 mg of LY3462817 administered as an IV infusion in 50 mg/mL in a 3-mL vial.

Number of subjects in period 1	Placebo	LY3462817 300 mg	LY3462817 700 mg
Started	24	25	49
Completed	22	23	46
Not completed	2	2	3
Consent withdrawn by subject	1	-	3
Physician decision	-	1	-
Adverse event, non-fatal	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received (0.9% sodium chloride solution) Placebo administered Intravenously.	
Reporting group title	LY3462817 300 mg
Reporting group description:	
Participants received 300 milligrams (mg) of LY3462817 administered Intravenously.	
Reporting group title	LY3462817 700 mg
Reporting group description:	
Participants received 700 mg of LY3462817 administered Intravenously.	

Reporting group values	Placebo	LY3462817 300 mg	LY3462817 700 mg
Number of subjects	24	25	49
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	55.8	50.1	50.5
standard deviation	± 11.1	± 15.8	± 11.2
Gender categorical Units: Subjects			
Female	19	20	43
Male	5	5	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	7	10	13
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	2
White	17	15	34
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Hungary	8	5	15
United States	4	5	9

Czechia	0	3	1
Poland	5	2	11
Mexico	7	10	13

Reporting group values	Total		
Number of subjects	98		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	82		
Male	16		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	30		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	66		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment Units: Subjects			
Hungary	28		
United States	18		
Czechia	4		
Poland	18		
Mexico	30		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received (0.9% sodium chloride solution) Placebo administered Intravenously.	
Reporting group title	LY3462817 300 mg
Reporting group description:	
Participants received 300 milligrams (mg) of LY3462817 administered Intravenously.	
Reporting group title	LY3462817 700 mg
Reporting group description:	
Participants received 700 mg of LY3462817 administered Intravenously.	

Primary: Change from Baseline on the Disease Activity Score Modified to Include the 28 Diarthrodial Joint Count–High-Sensitivity C-Reactive Protein (DAS28-hsCRP)

End point title	Change from Baseline on the Disease Activity Score Modified to Include the 28 Diarthrodial Joint Count–High-Sensitivity C-Reactive Protein (DAS28-hsCRP)

End point description:

Disease Activity Score (DAS) based on a 28 joint count hsCRP consisted of composite numerical score of the following variables: tender joint count (TJC28), swollen joint count (SJC28), hsCRP (mg/mL), and participant's global assessment of disease activity. DAS28-hsCRP was calculated using following formula: DAS28-hsCRP equals to (=) 0.56*square root (sqrt) (TJC28) plus (+) 0.28*sqrt (SJC28)+ 0.014* participant's global assessment of disease activity + 0.36*natural log(hsCRP+1) +0.96. Scores ranged 1.0-9.4, where lower scores indicated less disease activity. Least Square Mean (LS Mean) was calculated using mixed model repeated measures (MMRM) with treatment, strata (previous RA therapy population), baseline value, visit, treatment-by-visit interaction as fixed factors.
Analysis Population Description (APD): All randomized participants who received at least one dose and had data for DAS28-hsCRP

End point type	Primary

End point timeframe:

Baseline, Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	22	42	
Units: Units on a scale				
least squares mean (standard error)	-0.99 (± 0.261)	-1.88 (± 0.249)	-2.09 (± 0.184)	

Statistical analyses

Statistical analysis title	Change from Baseline on the DAS28-hsCRP
Comparison groups	Placebo v LY3462817 300 mg

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.361

Statistical analysis title	Change from Baseline on the DAS28-hsCRP
Comparison groups	Placebo v LY3462817 700 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	-0.46
Variability estimate	Standard error of the mean
Dispersion value	0.32

Secondary: Percentage of Participants Achieving 20% Improvement in American College of Rheumatology Criteria (ACR20)

End point title	Percentage of Participants Achieving 20% Improvement in American College of Rheumatology Criteria (ACR20)

End point description:

ACR responders are participants with at least 20% improvement from baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index (HAQ-DI) which measures participants perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Patient's Assessment of Pain-Visual Analog Scale (Pain-VAS), Patient’s Global Assessment of Disease Activity (PaGADA_VAS), and Physician’s Global Assessment of Disease Activity (PhGADA_VAS).
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	25	49	
Units: Percentage of Participants				
number (confidence interval 95%)	41.7 (21.9 to 61.4)	44.0 (24.5 to 63.5)	71.4 (58.8 to 84.1)	

Statistical analyses

Statistical analysis title	Percentage of Participants Achieving ACR20
Comparison groups	Placebo v LY3462817 300 mg
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.997
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	3.44

Statistical analysis title	Percentage of Participants Achieving ACR20
Comparison groups	Placebo v LY3462817 700 mg
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	10.4

Secondary: Percentage of Participants Achieving 70% Improvement in American

College of Rheumatology Criteria (ACR70)	
End point title	Percentage of Participants Achieving 70% Improvement in American College of Rheumatology Criteria (ACR70)

End point description:

ACR responders are participants with at least 70% improvement from baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index (HAQ-DI) which measures participants perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Patient's Assessment of Pain-Visual Analog Scale (Pain-VAS), Patient's Global Assessment of Disease Activity (PaGADA_VAS), and Physician's Global Assessment of Disease Activity (PhGADA_VAS).
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	25	49	
Units: Percentage of Participants				
number (confidence interval 95%)	16.7 (1.8 to 31.6)	4.0 (0 to 11.7)	20.4 (9.1 to 31.7)	

Statistical analyses

Statistical analysis title	Percentage of Participants Achieving ACR70
Comparison groups	Placebo v LY3462817 300 mg
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	2.25

Statistical analysis title	Percentage of Participants Achieving ACR70
Comparison groups	Placebo v LY3462817 700 mg

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.661
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	5.61

Secondary: Percentage of Participants Achieving 50% Improvement in American College of Rheumatology Criteria (ACR50)

End point title	Percentage of Participants Achieving 50% Improvement in American College of Rheumatology Criteria (ACR50)

End point description:

ACR responders are participants with at least 50% improvement from baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: Health Assessment Questionnaire-Disability Index (HAQ-DI) which measures participants perceived degree of difficulty performing daily activities, acute phase reactant as measured by hsCRP, Patient's Assessment of Pain-Visual Analog Scale (Pain-VAS), Patient's Global Assessment of Disease Activity (PaGADA_VAS), and Physician's Global Assessment of Disease Activity (PhGADA_VAS).
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	25	49	
Units: Percentage of Participants				
number (confidence interval 95%)	20.8 (4.6 to 37.1)	20.0 (4.3 to 35.7)	38.8 (25.1 to 52.4)	

Statistical analyses

Statistical analysis title	Percentage of Participants Achieving ACR50
Comparison groups	Placebo v LY3462817 300 mg

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.965
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	4.28

Statistical analysis title	Percentage of Participants Achieving ACR50
Comparison groups	Placebo v LY3462817 700 mg
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.098
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	10.33

Secondary: Change from Baseline for Mean Simplified Disease Activity Index (SDAI)

End point title	Change from Baseline for Mean Simplified Disease Activity Index (SDAI)

End point description:

The SDAI is a tool for measurement of disease activity in RA that integrates measures of physical examination, acute phase response, patient self-assessment, and evaluator assessment. The SDAI is calculated by adding together scores from 1) TJC28 (0 to 28), 2) SJC28 (0 to 28), 3) acute phase response using C-reactive protein (0.1 to 10.0 mg/dL), 4) Patient's Global Assessment of Disease Activity using VAS (0 to 10 cm), and 5) Physician's Global Assessment of Disease Activity using VAS (0 to 10 cm). Total Score scale range is 0 (remission) to 86 (high disease activity). LS Mean was calculated using mixed model repeated measures (MMRM) with treatment, strata (previous RA therapy population), baseline value, visit, treatment-by-visit interaction as fixed factors.
APD: All randomized participants who received at least one dose and had data for SDAI.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	42	
Units: units on a scale				
least squares mean (standard error)	-13.80 (± 2.664)	-25.06 (± 2.571)	-26.90 (± 1.880)	

Statistical analyses

Statistical analysis title	Change from Baseline for SDAI
Comparison groups	Placebo v LY3462817 300 mg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-11.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.65
upper limit	-3.87
Variability estimate	Standard error of the mean
Dispersion value	3.71

Statistical analysis title	Change from Baseline for SDAI
Comparison groups	Placebo v LY3462817 700 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.61
upper limit	-6.6
Variability estimate	Standard error of the mean
Dispersion value	3.265

Secondary: Change from Baseline for Mean Clinical Disease Activity Index (CDAI)

End point title	Change from Baseline for Mean Clinical Disease Activity Index (CDAI)

End point description:

The CDAI is a tool for measurement of disease activity in RA that does not require a laboratory component and was scored by the investigative site. It integrates TJC28 (scored 0-28 with higher scores indicating higher disease activity), SJC28 (scored 0-28 with higher scores indicating higher disease activity), Patient's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity), and Physician's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity). The CDAI is calculated by summing the values of the 4 components. CDAI scores range from 0 to 76; lower scores indicated lower disease activity. A negative change from baseline indicates improvement in condition. LS Mean was calculated using MMRM with treatment, strata (previous RA therapy population), baseline value, visit, treatment-by-visit interaction as fixed factors.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	44	
Units: units on a scale				
least squares mean (standard error)	-13.75 (± 2.709)	-24.06 (± 2.628)	-25.51 (± 1.854)	

Statistical analyses

Statistical analysis title	Change from Baseline for CDAI
Comparison groups	Placebo v LY3462817 300 mg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.83
upper limit	-2.77
Variability estimate	Standard error of the mean
Dispersion value	3.782

Statistical analysis title	Change from Baseline for CDAI
Comparison groups	Placebo v LY3462817 700 mg

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-11.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.29
upper limit	-5.22
Variability estimate	Standard error of the mean
Dispersion value	3.282

Secondary: Change From Baseline in Mental Component Score (MCS), Physical Component Score (PCS) of the Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Acute (SF-36v2 Acute)

End point title	Change From Baseline in Mental Component Score (MCS), Physical Component Score (PCS) of the Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Acute (SF-36v2 Acute)

End point description:

The SF-36 is a health-related survey that assesses participant's health status and consists of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems, role limitations due to emotional problems, general health, mental health, social functioning, and vitality. The 8 domains are combined to form 2 component scores mental (MCS) and physical (PCS). MCS consisted of social functioning, vitality, mental health, and role-emotional scales. PCS consisted of physical functioning, bodily pain, role-physical, and general health scales. Each domain is scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status. LS mean was determined by ANCOVA with factors for treatment and previous RA therapy population included as fixed factors,

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	LY3462817 300 mg	LY3462817 700 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	23	47	
Units: Units on a scale				
least squares mean (standard error)				
PCS	5.01 (± 1.711)	7.03 (± 1.633)	6.43 (± 1.165)	
MCS	3.48 (± 1.715)	0.55 (± 1.630)	4.64 (± 1.166)	

Statistical analyses

Statistical analysis title	Mental Component Score (MCS)
Comparison groups	Placebo v LY3462817 300 mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.218
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.63
upper limit	1.77
Variability estimate	Standard error of the mean
Dispersion value	2.365

Statistical analysis title	Mental Component Score (MCS)
Comparison groups	Placebo v LY3462817 700 mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.578
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.95
upper limit	5.26
Variability estimate	Standard error of the mean
Dispersion value	2.065

Statistical analysis title	Physical Component Score (PCS)
Comparison groups	Placebo v LY3462817 300 mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.396
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.69
upper limit	6.73
Variability estimate	Standard error of the mean
Dispersion value	2.368

Secondary: Pharmacokinetics (PK): Observed Concentration of LY3462817

End point title	Pharmacokinetics (PK): Observed Concentration of

End point description:

PK: Observed Concentration of LY3462817

End point type	Secondary

End point timeframe:

Week 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 analysis is for LY3462817

End point values	LY3462817 300 mg	LY3462817 700 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	49		
Units: nanograms per milliliter				
median (confidence interval 95%)	7970 (1290 to 17100)	15600 (1820 to 36600)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline, up to Week 12

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	LY3462817 700 mg
Reporting group description: -	
Reporting group title	LY3462817 300 mg

Reporting group description: -

Serious adverse events	Placebo	LY3462817 700 mg	LY3462817 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Endocrine disorders			
hypothyroidism			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	LY3462817 700 mg	LY3462817 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 24 (37.50%)	13 / 49 (26.53%)	8 / 25 (32.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

b-cell lymphoma			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Investigations			
weight increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 24 (8.33%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Surgical and medical procedures			
tooth extraction			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
allodynia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
dizziness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
headache			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
hypoaesthesia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
pyrexia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
nausea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	4 / 49 (8.16%)	0 / 25 (0.00%)
occurrences (all)	0	4	0
vomiting			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
dermatitis atopic			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
onychoclasis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
pruritus			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	1	3	0

Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
back pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
osteoarthritis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
rheumatoid arthritis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
covid-19			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
gastroenteritis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
helicobacter infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
herpes simplex			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
mastitis			

alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
nasopharyngitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	1 / 49 (2.04%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
rhinitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
sinusitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
skin bacterial infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 49 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
tooth abscess			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 49 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
urinary tract infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
upper respiratory tract infection bacterial			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed[1]	0 / 19 (0.00%)	1 / 43 (2.33%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
diabetes mellitus			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
dyslipidaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 24 (8.33%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	2	1	0
hyperglycaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 49 (2.04%)	0 / 25 (0.00%)
occurrences (all)	0	1	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2020	Protocol Amendment (a) • Participants on placebo will not be allowed to crossover to LY3462817 at any point during the study. • Added requirement of an Interim Analysis of Study KDAC data collected prior to proceeding to Period 2. • Standard of Care (SOC) therapy to be allowed to begin at Week 14. • All participants on placebo will receive SOC starting at Week 14 (Visit 7). • Removed Rescue Therapy wording • Patients who do not achieve Low Disease Activity will be removed from LY3462817 and switched to standard of care. • Patients who do achieve Low Disease Activity will be allowed LY3462817 until week 24.
11 December 2020	Protocol amendment (b): The protocol was amended to clarify study procedures and statistical considerations.

Notes:

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.

No adjustment for multiplicity was made. For assessments beyond the primary endpoint, nominal p-values are reported.

Notes: