Clinical trial results:
Pharmacokinetic Evaluations of Tabalumab Following Subcutaneous Administration by Prefilled syringe or Auto-Injector in Patients with Rheumatoid Arthritis Who Have Had an Inadequate Response to Methotrexate.

Summary

EudraCT number	2012-001618-40
Trial protocol	CZ PL
Global end of trial date	19 August 2013

Results information

Result version number	v1 (current)
This version publication date	09 April 2018
First version publication date	09 April 2018

Trial information

Trial identification

Sponsor protocol code	H9B-MC-BCEF

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01676701
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14598

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, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	19 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study was to include a 12-week treatment period, optional 40-week safety extension, and post-treatment follow-up (at least 24 weeks). At the time of early study termination, all participants who had received tabalumab discontinued dosing and then completed the post-treatment follow-up period. No one entered the 40-week safety extension period.

This study has been terminated not based on safety concerns, but due to insufficient efficacy.

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	17 September 2012
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	Czech Republic: 3
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	29
EEA total number of subjects	3

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)	22

From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No text entered.

Pre-assignment

Screening details:

No text entered.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tabalumab Auto-Injector

Arm description:

Tabalumab: Using auto-injectors, participants received a 180 milligram (mg) loading dose at Week 0 as 2 subcutaneous (SC) injections (90 mg each). Participants also received a 90 mg SC injection every 2 weeks (Q2W) until early study termination (up to Week 6).

Arm type	Experimental
Investigational medicinal product name	Tabalumab Auto-Injector
Investigational medicinal product code	
Other name	LY2127399
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tabalumab 180 milligram (mg) loading dose administered using auto-injectors at Week 0 as 2 subcutaneous (SC) injections (90 mg each), followed by a 90 mg SC injection every 2 weeks (Q2W) up to Week 12.

Arm title	Tabalumab Prefilled Syringe

Arm description:

Tabalumab: Using prefilled syringes, participants received a 180 mg loading dose administered at Week 0 as 2 SC injections (90 mg each). Participants also received a 90 mg SC injection Q2W until early study termination (up to Week 6).

Arm type	Experimental
Investigational medicinal product name	Tabalumab Prefilled Syringe
Investigational medicinal product code	
Other name	LY2127399
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tabalumab 180 mg loading dose administered using prefilled syringes at Week 0 as 2 SC injections (90 mg each), followed by a 90 mg SC injection Q2W up to Week 12.

Number of subjects in period 1[1]	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe
Started	4	4
Received at Least 1 Dose of Study Drug	4	4
Completed Post-Treatment Follow-Up	4	4
Completed	0	0
Not completed	4	4
Sponsor Decision	3	4
Protocol deviation	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of participants entered trial are 29 and the number of participants entered treatment are 4.

Baseline characteristics

Reporting groups	
Reporting group title	Tabalumab Auto-Injector
Reporting group description:	
Tabalumab: Using auto-injectors, participants received a 180 milligram (mg) loading dose at Week 0 as 2 subcutaneous (SC) injections (90 mg each). Participants also received a 90 mg SC injection every 2 weeks (Q2W) until early study termination (up to Week 6).	
Reporting group title	Tabalumab Prefilled Syringe
Reporting group description:	
Tabalumab: Using prefilled syringes, participants received a 180 mg loading dose administered at Week 0 as 2 SC injections (90 mg each). Participants also received a 90 mg SC injection Q2W until early study termination (up to Week 6).	

Reporting group values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe	Total
Number of subjects	4	4	8
Age categorical Units: Subjects			
43.3 to 65.4 years	4	4	8
Gender categorical Units: Subjects			
Female	3	3	6
Male	1	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	4	3	7
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	4	3	7
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
United States	4	4	8

End points

End points reporting groups

Reporting group title	Tabalumab Auto-Injector

Reporting group description:

Tabalumab: Using auto-injectors, participants received a 180 milligram (mg) loading dose at Week 0 as 2 subcutaneous (SC) injections (90 mg each). Participants also received a 90 mg SC injection every 2 weeks (Q2W) until early study termination (up to Week 6).

Reporting group title	Tabalumab Prefilled Syringe

Reporting group description:

Tabalumab: Using prefilled syringes, participants received a 180 mg loading dose administered at Week 0 as 2 SC injections (90 mg each). Participants also received a 90 mg SC injection Q2W until early study termination (up to Week 6).

Primary: Pharmacokinetics (PK): Maximum Serum Concentration (Cmax) of Tabalumab After Loading Dose

End point title	Pharmacokinetics (PK): Maximum Serum Concentration (Cmax) of Tabalumab After Loading Dose[1]

End point description:

No participant had outcome measure data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Primary

End point timeframe:

Days 4, 7, 9, 11, and 14 after loading dose administered

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 end point data analyzed due to the termination of the trial and an insufficient sample size.

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: insufficient sample size				

Notes:

[2] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[3] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Area Under the Concentration Time Curve From Time 0 to 14 Days [AUC(0-14)]

End point title	PK: Area Under the Concentration Time Curve From Time 0 to 14 Days [AUC(0-14)]

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Days 4, 7, 9, 11, and 14 after loading dose administered

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: insufficient sample size.				

Notes:

[4] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[5] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 12-Week Endpoint in Achieving American College of Rheumatology (ACR) Core Set

End point title	Change From Baseline to 12-Week Endpoint in Achieving American College of Rheumatology (ACR) Core Set

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: insufficient sample size.				

Notes:

[6] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[7] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR Response

End point title	Percentage of Participants Achieving ACR Response

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: insufficient sample size				

Notes:

[8] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[9] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to 12-Week Endpoint in American College of Rheumatology (ACR-N) Index

End point title	Percent Change From Baseline to 12-Week Endpoint in American College of Rheumatology (ACR-N) Index

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: insufficient sample size				

Notes:

[10] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[11] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 12-Week Endpoint in Disease Activity Score Based on a 28-Joint Count and C-Reactive Protein (DAS28-CRP) Level

End point title	Change From Baseline to 12-Week Endpoint in Disease Activity Score Based on a 28-Joint Count and C-Reactive Protein (DAS28-CRP) Level

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: insufficient sample size				

Notes:

[12] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[13] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving European League Against Rheumatism Responder Index Based on the 28-Joint Count (EULAR-28)

End point title	Percentage of Participants Achieving European League Against Rheumatism Responder Index Based on the 28-Joint Count (EULAR-28)

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: insufficient sample size				

Notes:

[14] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[15] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Developing Anti-Tabalumab Antibodies

End point title	Number of Participants Developing Anti-Tabalumab Antibodies

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: insufficient sample size				

Notes:

[16] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[17] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Operation Failures

End point title	Number of Operation Failures

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Week 12

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: insufficient sample size				

Notes:

[18] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[19] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Score in Subcutaneous Administration Assessment Questionnaire (SQAAQ)

End point title	Change From Baseline Score in Subcutaneous Administration Assessment Questionnaire (SQAAQ)

End point description:

No end point data analyzed due to the termination of the trial and an insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4 and 8

End point values	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: insufficient sample size				

Notes:

[20] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

[21] - No end point data analyzed due to the termination of the trial and an insufficient sample size.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
H9B-MC-BCEF	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Tabalumab Auto-Injector
Reporting group description: -	
Reporting group title	Tabalumab Prefilled Syringe
Reporting group description: -	

Serious adverse events	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Tabalumab Auto-Injector	Tabalumab Prefilled Syringe	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
Infections and infestations			
Gastric Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Due to early termination of the trial, no participant had outcome measure data analyzed. Participants who received study treatment had disposition, demographic, and adverse event data reported.

Notes: