# 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<br>Units: Subjects | | | |
| 43.3 to 65.4 years | 4 | 4 | 8 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 3 | 3 | 6 |
| Male | 1 | 1 | 2 |
| Ethnicity (NIH/OMB)<br>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)<br>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<br>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: