Clinical trial results:
A Phase 1, Open-Label, Multi-Center, Two-Part, Single-Dose, Parallel Design, Safety, Tolerance, and Pharmacokinetic Study of Orally and Intravenously Administered TR-701 FA in 12 to 17 Year Old Adolescent Patients

Summary

EudraCT number	2015-002780-42
Trial protocol	Outside EU/EEA
Global end of trial date	24 September 2011

Results information

Result version number	v2 (current)
This version publication date	26 May 2016
First version publication date	02 August 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1986-026

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01156077
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Trius Therapeutics
Sponsor organisation address	6310 Nancy Ridge Drive, San Diego, United States,
Public contact	Medical Director, Trius Therapeutics, 011 8584520370,
Scientific contact	Medical Director, Trius Therapeutics, 011 8584520370,
Sponsor organisation name	Cubist Pharmaceuticals, Inc
Sponsor organisation address	65 Hayden Avenue, Lexington, United States,
Public contact	Medical Director, Cubist Pharmaceuticals, Inc, 011 781860-8660,
Scientific contact	Medical Director, Cubist Pharmaceuticals, Inc, 011 781860-8660,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 July 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 September 2011
Global end of trial reached?	Yes
Global end of trial date	24 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the single-dose pharmacokinetics (PK) of TR-701 free acid (FA) and its active metabolite, TR-700, when administered orally and intravenously (IV) in 12- to 17-year-old adolescent subjects

Protection of trial subjects:

This study was conducted in accordance with current United States Food and Drug Administration regulations, International Conference of Harmonisation Good Clinical Practice guidelines, and the Institutional Review Board and local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2010
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	United States: 20
Worldwide total number of subjects	20
EEA total number of subjects	0

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)	20
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible subjects in the study were to be 12- to 17-year-old adolescents who were receiving prophylaxis for or who had a confirmed or suspected gram-positive bacterial infection and were receiving concurrent antibiotic treatment with gram-positive antibacterial activity.

Period 1

Period 1 title	Baseline Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	oral TR-701 FA

Arm description:

Single oral dose of 200 milligrams (mg) TR-701 free acid (FA)

Arm type	Experimental
Investigational medicinal product name	TR-701
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

single dose of 200-milligrams (mg) TR-701 free acid (FA) administered as an oral tablet

Arm title	IV TR-701 FA

Arm description:

Single IV infusion of 200 mg TR-701 FA

Arm type	Experimental
Investigational medicinal product name	TR-701
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of 200 mg TR-701 FA

Number of subjects in period 1	oral TR-701 FA	IV TR-701 FA
Started	10	10
Received at least 1 dose of study drug	10	10
Completed	10	10

Baseline characteristics

Reporting groups	
Reporting group title	oral TR-701 FA
Reporting group description:	
Single oral dose of 200 milligrams (mg) TR-701 free acid (FA)	
Reporting group title	IV TR-701 FA
Reporting group description:	
Single IV infusion of 200 mg TR-701 FA	

Reporting group values	oral TR-701 FA	IV TR-701 FA	Total
Number of subjects	10	10	20
Age categorical Units: Subjects			
Age continuous			
There was 1 subject in the IV TR-701 FA treatment group who as 11 years-old at the time of initial enrollment but 12 years old at the time of study drug administration. This subject is reported as 12 years old in the IV TR-701 FA treatment group.			
Units: years			
arithmetic mean	15	14	
full range (min-max)	12 to 17	12 to 17	-
Gender categorical Units: Subjects			
Female	1	3	4
Male	9	7	16

End points

End points reporting groups

Reporting group title	oral TR-701 FA
Reporting group description:	
Single oral dose of 200 milligrams (mg) TR-701 free acid (FA)	
Reporting group title	IV TR-701 FA
Reporting group description:	
Single IV infusion of 200 mg TR-701 FA	

Primary: Mean and standard deviation (SD) Plasma Pharmacokinetic Parameter Data for TR-701: Cmax

End point title	Mean and standard deviation (SD) Plasma Pharmacokinetic Parameter Data for TR-701: Cmax
End point description:	
Cmax=maximum observed plasma concentration ng/mL=nanograms per milliliter	
End point type	Primary
End point timeframe:	
Two days	

End point values	oral TR-701 FA	IV TR-701 FA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[1]	10[2]		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax	2231 (± 549)	3854 (± 1506)		

Notes:

[1] - Subjects who received at least 1 dose of study drug with evaluable PK data

[2] - Subjects who received at least 1 dose of study drug with evaluable PK data

Statistical analyses

Statistical analysis title	Statistical Analysis of TR-700 PK Data--Cmax
Statistical analysis description:	
Ratio of parameter means for natural log transformed parameter (expressed as a percent). Natural log transformed ratios transformed back to the linear scale. 90% confidence interval for ratio of parameter means of natural log transformed parameter (expressed as a percent). Natural log transformed confidence limits transformed back to the linear scale	
Comparison groups	oral TR-701 FA v IV TR-701 FA
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Ratio of parameter means for natural log
Point estimate	59.34

Confidence interval	
level	90 %
sides	2-sided
lower limit	47.5
upper limit	74.12

Notes:

[3] - Analysis of variance (ANOVA)

Primary: Mean (SD) Plasma Pharmacokinetic Parameter Data for TR-701: AUC (0-∞)

End point title	Mean (SD) Plasma Pharmacokinetic Parameter Data for TR-701: AUC (0-∞)

End point description:

AUC (0-∞)=area under the plasma concentration-time curve extrapolated to infinity
ng*hr/mL=nanograms times hours per milliliter

End point type	Primary

End point timeframe:

Two days

End point values	oral TR-701 FA	IV TR-701 FA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[4]	10[5]		
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
AUC(0- ∞)	25205 (± 9153)	27820 (± 7282)		

Notes:

[4] - Subjects who received at least 1 dose of study drug with evaluable PK data

[5] - Subjects who received at least 1 dose of study drug with evaluable PK data

Statistical analyses

Statistical analysis title	Statistical Analysis of TR-700 PK Data--AUC (0 -∞)

Statistical analysis description:

Ratio of parameter means for natural log transformed parameter (expressed as a percent). Natural log transformed ratios transformed back to the linear scale. 90% confidence interval for ratio of parameter means of natural log transformed parameter (expressed as a percent). Natural log transformed confidence limits transformed back to the linear scale.

Comparison groups	oral TR-701 FA v IV TR-701 FA
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Ratio of parameter means for natural log
Point estimate	88.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	70.37
upper limit	112.11

Notes:
[6] - analysis of variance (ANOVA)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Screening (Study Day -3 to 1) through the Final Visit (Study Day 2)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1
Reporting groups	
Reporting group title	IV TR-701 FA
Reporting group description: -	
Reporting group title	oral TR-701 FA
Reporting group description: -	

Serious adverse events	IV TR-701 FA	oral TR-701 FA	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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	IV TR-701 FA	oral TR-701 FA	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)	1 / 10 (10.00%)	
Investigations			
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
PROCEDURAL PAIN			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
DIZZINESS			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
CONSTIPATION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (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

None reported