Clinical trial results:
A Phase 3 Randomized, Double Blind Study Assessing the Efficacy and Safety of PF-06410293 and Adalimumab in Combination With Methotrexate in Subjects With Moderately to Severely Active Rheumatoid Arthritis Who Have Had an Inadequate Response to Methotrexate

Summary

EudraCT number	2014-000352-29
Trial protocol	CZ EE LT HU GB DE ES FR BG HR
Global end of trial date	

Results information

Result version number	v1
This version publication date	13 September 2017
First version publication date	13 September 2017

Trial information

Trial identification

Sponsor protocol code	B5381002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02480153
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.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	Interim
Date of interim/final analysis	03 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the treatment efficacy between adalimumab-Pfizer (PF-06410293) and adalimumab-EU (adalimumab sourced from the European Union) in subjects with moderately to severely active rheumatoid arthritis who were treated with adalimumab in combination with methotrexate.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy:

Subjects continued their stable background regimen of oral or intramuscular methotrexate (10 to 25 mg/week, with the exception of 6 to 25 mg/week in geographic regions where 6 mg/week was a recommended initial dose by local guidance or standard of care) throughout the study.

Evidence for comparator:

This study was designed to compare the treatment efficacy between PF-06410293 and adalimumab-EU; therefore, adalimumab-EU was used as the comparator.

Actual start date of recruitment	25 June 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Bulgaria: 37
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Czech Republic: 31
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Georgia: 33
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Japan: 17
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Lithuania: 30
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	New Zealand: 4

Country: Number of subjects enrolled	Peru: 24
Country: Number of subjects enrolled	Poland: 87
Country: Number of subjects enrolled	Russian Federation: 56
Country: Number of subjects enrolled	Serbia: 35
Country: Number of subjects enrolled	South Africa: 15
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Ukraine: 66
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 75
Worldwide total number of subjects	597
EEA total number of subjects	241

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)	480
From 65 to 84 years	117
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1231 potential participants were screened after signing an informed consent form, of whom 597 participants were randomized to receive study treatment.

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	PF-06410293

Arm description:

Participants received subcutaneous (SC) injection of PF-06410293 at a dose of 40 mg every other week.

Arm type	Experimental
Investigational medicinal product name	PF-06410293
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06410293 was self-administered by subjects via subcutaneous (SC) injection at a dose of 40 mg every other week. The first injection was performed in the abdominal region at the site under the supervision of the investigator or designee. Thereafter, the subject selected a regular day of the week for their subsequent injections at home.

Arm title	Adalimumab-EU

Arm description:

Participants received subcutaneous (SC) injection of adalimumab (adalimumab sourced from the European Union) at a dose of 40 mg every other week.

Arm type	Active comparator
Investigational medicinal product name	Adalimumba-EU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab-EU (adalimumab sourced from the European Union) was self-administered by subjects via subcutaneous (SC) injection at a dose of 40 mg every other week. The first injection was performed in the abdominal region at the site under the supervision of the investigator or designee. Thereafter, the subject selected a regular day of the week for their subsequent injections at home.

Number of subjects in period 1	PF-06410293	Adalimumab-EU
Started	297	300
Received treatment	297	299
Completed	286	273
Not completed	11	27
Randomized but not treated	-	1
Withdrew treatment; continued in study	6	14
Discontinued from treatment and study	5	12

Baseline characteristics

Reporting groups	
Reporting group title	PF-06410293
Reporting group description:	
Participants received subcutaneous (SC) injection of PF-06410293 at a dose of 40 mg every other week.	
Reporting group title	Adalimumab-EU
Reporting group description:	
Participants received subcutaneous (SC) injection of adalimumab (adalimumab sourced from the European Union) at a dose of 40 mg every other week.	

Reporting group values	PF-06410293	Adalimumab-EU	Total
Number of subjects	297	300	597
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	245	235	480
From 65-84 years	52	65	117
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	51.5	53.5	
standard deviation	± 13.6	± 12.9	-
Gender, Male/Female			
Units: Subjects			
Female	241	229	470
Male	56	71	127

End points

End points reporting groups

Reporting group title	PF-06410293
Reporting group description:	
Participants received subcutaneous (SC) injection of PF-06410293 at a dose of 40 mg every other week.	
Reporting group title	Adalimumab-EU
Reporting group description:	
Participants received subcutaneous (SC) injection of adalimumab (adalimumab sourced from the European Union) at a dose of 40 mg every other week.	

Primary: Percentage of Subjects with an American College of Rheumatology 20% (ACR20) Response at Week 12 in the Intent-to-Treat (ITT) Population

End point title	Percentage of Subjects with an American College of Rheumatology 20% (ACR20) Response at Week 12 in the Intent-to-Treat (ITT) Population
End point description:	
ACR20 is a categorical variable indicating a 20% or greater improvement in tender and swollen joint counts and 20% or greater improvement in 3 of the 5 other ACR-core set measures: subject's assessment of arthritis pain; subject's global assessment of arthritis; physician's global assessment of arthritis; high sensitivity C-reactive protein (hs-CRP); and Health Assessment Questionnaire - Disability Index (HAQ-DI). The intent-to-treat (ITT) population was defined as all subjects who were randomized to study treatment. Non-responder imputation was applied.	
End point type	Primary
End point timeframe:	
Weeks 2, 4, 6, 8, 12, 18 and 26	

End point values	PF-06410293	Adalimumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297	300		
Units: percentage of subjects				
number (not applicable)	68.35	71.33		

Statistical analyses

Statistical analysis title	Statistical analysis with 95% CI
Statistical analysis description:	
Confidence interval (CIs) calculated by the score statistic method were used for the inference of the equivalence for ACR20 at Week 12. Therapeutic equivalence could be established if the 2-sided 95% CI fell within (-14%, 14%) and 2-sided 90% CI fell within (-12%, 15%). Non-responder imputation was applied. Comparisons between treatments were computed as PF-06410293 versus Adalimumab-EU.	
Comparison groups	PF-06410293 v Adalimumab-EU

Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	proportion difference
Point estimate	-2.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.38
upper limit	4.44

Notes:

[1] - For subjects who discontinued from treatment prior to Week 12 or had a missing ACR20 at Week 12, a non-responder was assigned to their Week 12 ACR20 assessment.

Statistical analysis title	Statistical analysis with 90% CI

Statistical analysis description:

Confidence interval (CIs) calculated by the score statistic method were used for the inference of the equivalence for ACR20 at Week 12.
Therapeutic equivalence could be established if the 2-sided 95% CI fell within (-14%, 14%) and 2-sided 90% CI fell within (-12%, 15%).
Non-responder imputation was applied. Comparisons between treatments were computed as PF-06410293 versus Adalimumab-EU.

Comparison groups	PF-06410293 v Adalimumab-EU
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	proportion difference
Point estimate	-2.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.25
upper limit	3.28

Notes:

[2] - For subjects who discontinued from treatment prior to Week 12 or had a missing ACR20 at Week 12, a non-responder was assigned to their Week 12 ACR20 assessment.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study treatment to Week 26 visit (pre-dose)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	PF-06410293
Reporting group description:	
Participants received subcutaneous (SC) injection of PF-06410293 at a dose of 40 mg every other week.	
Reporting group title	Adalimumab-EU
Reporting group description:	
Participants received subcutaneous (SC) injection of adalimumab (adalimumab sourced from the European Union) at a dose of 40 mg every other week.	

Serious adverse events	PF-06410293	Adalimumab-EU	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 297 (4.04%)	13 / 299 (4.35%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibroadenoma of breast			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			

subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 297 (0.00%)	2 / 299 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Intentional self-injury			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			

subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Toxic skin eruption			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Bronchitis			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 297 (0.00%)	2 / 299 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 297 (0.34%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	0 / 297 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PF-06410293	Adalimumab-EU	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 297 (7.07%)	18 / 299 (6.02%)	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	21 / 297 (7.07%)	18 / 299 (6.02%)	
occurrences (all)	22	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2014	Added urinalysis at Week 52 and fixed study day for follow up visit; Asia region was split to Japan and (South Korea + Taiwan) for randomization stratification; decreased entry methotrexate dose to 6 mg/week from 8 mg/week in geographic regions where 6 mg/week was a recommended initial dose by local guidance or standard of care; removed permission for use of any second disease modifying anti-rheumatic drug (DMARD) therapy, including sulfasalazine and/or anti-malarial drug during trial, and 4-week washout was required; Added recording of injection times after pharmacokinetic (PK) samples, and added time to 1 other injection before Week 12 primary endpoint that would not otherwise be recorded; added additional anti-drug antibody (ADA) sample at Week 6 as requested by the European Medicines Agency (EMA); changed ADA analysis plan to run all samples in both ADA assays as requested by the US Food and Drug Administration (FDA); added a return visit at Week 26 in subjects who withdrew before Week 26, as requested by the FDA; added follow-up telephone calls at Weeks 4 and 8 in subjects who withdrew before that, as requested by the EMA; added the option for an additional safety visit including laboratories at the discretion of the investigator, in case of any significant safety concerns at a phone follow-up, as requested by the EMA; updated permitted opioid drug tables to specify types of opioids allowed as background therapies versus those allowed as rescue therapies.
08 September 2014	Added safety telephone follow-up contact 16 weeks after final dose of study drug; added exclusion of subjects with prior history of severe allergic or anaphylactic reaction to a biologic drug, and clarified the washout period for prior investigational drugs to be the longer of the 2 stated options (4 weeks or 5 half-lives); pregnancy was added to treatment withdrawal criteria; added clarification and cross-references placed in protocol.
25 September 2014	Changed immunogenicity testing plan so that all immunogenicity samples were to be tested for ADA using a single, validated electrochemiluminescent (ECL) immunoassay for ADA against PF-06410293, instead of 2 assays; added another ADA sample, with a companion PK sample, in both treatment period 2(TP2) and TP3 for monitoring of post switch immunogenicity time course; modified follow-up procedures for subjects who discontinued before Week 26 to require more on-site visits in TP1; modified wording for subject discontinuation due to lack of efficacy to allow some investigator discretion; specified requirements for immediate release narcotic; added supplemental urine pregnancy testing as requested by Canadian regulatory authorities.
15 July 2015	Added DMARDs to the DMARD Washout Periods table.
13 November 2015	Modified optional isoniazid prophylaxis for high-risk subjects to be globally available where standard of care during adalimumab (study drug) treatment; added an appendix describing additional GCP and inspection responsibilities; clarified that the subject would select the most appropriate form of birth control in consultation with the investigator or designee; corrected the End of Treatment (EOT)/Early Termination (ET) urine pregnancy test to occur on Week 78/Visit 18 and not during Visit 17 at Week 76; clarified maximal paracetamol dose for chronic dosing (comparable to maximal chronic acetaminophen dose already listed); for RA flare treatment, added 1 oral corticosteroid (7 day) course after study Week 26 and altered the maximal intra articular corticosteroid dose to 40 mg methylprednisolone (or equivalent) per injection.
16 May 2016	Added a prefilled pen (PFP) sub-study during TP3 to evaluate the success of PF-06410293 administration by PFP.

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.

Only data from the first 26-week treatment period (from baseline to Week 26 pre-dose) are presented for this ongoing study. This report will be updated after completion of the study.

Notes: