Clinical trial results:
A Multicenter, Open-Label, Single-arm Study to Assess the Efficacy and Safety of PF-06462700 Administered Intravenously at 40 mg/kg/day for 4 Days in Japanese Participants With Moderate and Above Aplastic Anemia

Summary

EudraCT number	2021-002155-11
Trial protocol	Outside EU/EEA
Global end of trial date	19 April 2021

Results information

Result version number	v1
This version publication date	21 October 2021
First version publication date	21 October 2021

Trial information

Trial identification

Sponsor protocol code	B5411003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04350606
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, NY 10017, United States,
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of PF- 06462700 administered intravenously at 40 mg/kg/day for 4 days in Japanese participants with moderate and above aplastic anemia.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 July 2020
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	Japan: 3
Worldwide total number of subjects	3
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)	1
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in single country from 25 July 2020 to 19 Apr 2021. Total 3 subjects signed the inform consent form (ICF). Out of which 0 subjects were screen failures, 3 actually enrolled into the study and assigned to a study treatment.

Period 1

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

Arms

Arm title	PF-06462700

Arm description:

Subjects aged 2 years or greater than (>) 2 years with moderate and above severity aplastic anemia received PF-06462700 at a dose of 40 milligram per kilogram per day (mg/kg/day), intravenously (IV) for 4 days. Subjects after treatment were followed up for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	PF-06462700
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06462700 dose of 40 mg/kg/day for 4 days.

Number of subjects in period 1	PF-06462700
Started	3
Treated	3
Follow-up	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	PF-06462700
Reporting group description:	
Subjects aged 2 years or greater than (>) 2 years with moderate and above severity aplastic anemia received PF-06462700 at a dose of 40 milligram per kilogram per day (mg/kg/day), intravenously (IV) for 4 days. Subjects after treatment were followed up for 24 weeks.	

Reporting group values	PF-06462700	Total	
Number of subjects	3	3	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	2	2	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	29.67		
standard deviation	± 16.56	-	
Gender Categorical Units: Subjects			
Female	2	2	
Male	1	1	
Race Units: Subjects			
White	0	0	
Black or African American	0	0	
Asian	3	3	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
More than one race	0	0	
Unknown or Not reported	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	3	3	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	PF-06462700

Reporting group description:

Subjects aged 2 years or greater than (>) 2 years with moderate and above severity aplastic anemia received PF-06462700 at a dose of 40 milligram per kilogram per day (mg/kg/day), intravenously (IV) for 4 days. Subjects after treatment were followed up for 24 weeks.

Primary: Number of Subjects With Hematologic Response at Week 12

End point title	Number of Subjects With Hematologic Response at Week 12[1]

End point description:

Hematologic response was considered to be "effective" when 2 or more of the following criteria were met: absolute neutrophil count greater than or equal to (>=) 500 per microliters, platelet count >=20,000 per microliters and reticulocyte count >=60,000 per microliters was observed. In this outcome measure, number of subjects with hematologic response classified as effective and not effective were reported. Improvement in counts that were dependent upon exogenously administered growth factors or transfusion, was not considered as fulfilling response criteria. Full analysis set (FAS) included subjects were assigned to investigational product and who took at least 1 dose of investigational

End point type	Primary

End point timeframe:

Week 12 Follow-up Visit

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 statistical analysis was planned for this endpoint

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Effective	2			
Not Effective	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Hematologic Response at Week 24

End point title	Number of Subjects With Hematologic Response at Week 24

End point description:

Hematologic response was considered to be "effective" when 2 or more of the following criteria were met: absolute neutrophil count >=500 per microliters, platelet count >=20,000 per microliters and reticulocyte count >=60,000 per microliters was observed. In this outcome measure, number of subjects with hematologic response classified as effective and not effective were reported. Improvement in counts that were dependent upon exogenously administered growth factors or transfusion, was not been considered as fulfilling response criteria. FAS included subjects were assigned to investigational product and who took at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:
Week 24 Follow-up Visit

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Effective	2			
Not Effective	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Neutrophil Count at Day 4, Weeks 1, 2, 4, 6, 8, 10, 12, 24

End point title	Absolute Neutrophil Count at Day 4, Weeks 1, 2, 4, 6, 8, 10, 12, 24

End point description:

FAS included subjects who were assigned to investigational product and who took at least 1 dose of investigational product. Here, "n" signifies the number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Treatment: Day 4; Follow-up: Week 1, 2, 4, 6, 8, 10, 12, 24

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Neutrophil cells per microliter				
Subject 1 : Day 4 (n=1)	300			
Subject 1 : Week 1 (n=1)	300			
Subject 1 : Week 2 (n=1)	700			
Subject 1 : Week 4 (n=1)	200			
Subject 1 : Week 6 (n=1)	700			
Subject 1 : Week 8 (n=1)	2100			
Subject 1 : Week 10 (n=1)	2400			
Subject 1 : Week 12 (n=1)	2300			
Subject 1 : Week 24 (n=1)	2700			
Subject 2 : Day 4 (n=1)	64			
Subject 2 : Week 1 (n=1)	252			
Subject 2 : Week 2 (n=1)	495			
Subject 2 : Week 4 (n=1)	814			
Subject 2 : Week 6 (n=1)	300			
Subject 2 : Week 8 (n=1)	450			

Subject 2 : Week 10 (n=1)	750			
Subject 2 : Week 12 (n=1)	450			
Subject 2 : Week 24 (n=1)	750			
Subject 3 : Day 4 (n=1)	8			
Subject 3 : Week 1 (n=1)	180			
Subject 3 : Week 2 (n=1)	258			
Subject 3 : Week 4 (n=1)	175			
Subject 3 : Week 6 (n=1)	1679			
Subject 3 : Week 8 (n=1)	2432			
Subject 3 : Week 10 (n=1)	4335			
Subject 3 : Week 12 (n=1)	5330			
Subject 3 : Week 24 (n=1)	1755			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet Count at Day 4, Weeks 1, 2, 4, 6, 8, 10, 12, 24

End point title	Platelet Count at Day 4, Weeks 1, 2, 4, 6, 8, 10, 12, 24

End point description:

FAS included subjects who were assigned to investigational product and who took at least 1 dose of investigational product. Here, "n" signifies the number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Treatment: Day 4; Follow-up: Week 1, 2, 4, 6, 8, 10, 12, 24

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Platelet cells per microliter				
Subject 1 : Day 4 (n=1)	34000			
Subject 1 : Week 1 (n=1)	23000			
Subject 1 : Week 2 (n=1)	9000			
Subject 1 : Week 4 (n=1)	11000			
Subject 1 : Week 6 (n=1)	22000			
Subject 1 : Week 8 (n=1)	46000			
Subject 1 : Week 10 (n=1)	72000			
Subject 1 : Week 12 (n=1)	77000			
Subject 1 : Week 24 (n=1)	139000			
Subject 2 : Day 4 (n=1)	34000			
Subject 2 : Week 1 (n=1)	8000			
Subject 2 : Week 2 (n=1)	56000			
Subject 2 : Week 4 (n=1)	15000			
Subject 2 : Week 6 (n=1)	21000			
Subject 2 : Week 8 (n=1)	21000			
Subject 2 : Week 10 (n=1)	37000			

Subject 2 : Week 12 (n=1)	47000			
Subject 2 : Week 24 (n=1)	58000			
Subject 3 : Day 4 (n=1)	21000			
Subject 3 : Week 1 (n=1)	7000			
Subject 3 : Week 2 (n=1)	40000			
Subject 3 : Week 4 (n=1)	9000			
Subject 3 : Week 6 (n=1)	8000			
Subject 3 : Week 8 (n=1)	36000			
Subject 3 : Week 10 (n=1)	45000			
Subject 3 : Week 12 (n=1)	88000			
Subject 3 : Week 24 (n=1)	16000			

Statistical analyses

No statistical analyses for this end point

Secondary: Reticulocyte Count at Day 4, Weeks 1, 2, 4, 6, 8, 10, 12, 24

End point title	Reticulocyte Count at Day 4, Weeks 1, 2, 4, 6, 8, 10, 12, 24

End point description:

FAS included subjects who were assigned to investigational product and who took at least 1 dose of investigational product. Here, "n" signifies the number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Treatment: Day 4; Follow-up: Week 1, 2, 4, 6, 8, 10, 12, 24

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Reticulocyte cells per microliter				
Subject 1 : Day 4 (n=1)	14100			
Subject 1 : Week 1 (n=1)	7350			
Subject 1 : Week 2 (n=1)	8840			
Subject 1 : Week 4 (n=1)	17780			
Subject 1 : Week 6 (n=1)	34650			
Subject 1 : Week 8 (n=1)	90090			
Subject 1 : Week 10 (n=1)	113600			
Subject 1 : Week 12 (n=1)	84300			
Subject 1 : Week 24 (n=1)	53760			
Subject 2 : Day 4 (n=1)	5000			
Subject 2 : Week 1 (n=1)	6000			
Subject 2 : Week 2 (n=1)	6000			
Subject 2 : Week 4 (n=1)	12000			
Subject 2 : Week 6 (n=1)	16000			
Subject 2 : Week 8 (n=1)	37000			
Subject 2 : Week 10 (n=1)	44000			
Subject 2 : Week 12 (n=1)	69000			

Subject 2 : Week 24 (n=1)	85000			
Subject 3 : Day 4 (n=1)	14400			
Subject 3 : Week 1 (n=1)	10800			
Subject 3 : Week 2 (n=1)	9600			
Subject 3 : Week 4 (n=1)	14700			
Subject 3 : Week 6 (n=1)	11200			
Subject 3 : Week 8 (n=1)	26300			
Subject 3 : Week 10 (n=1)	230200			
Subject 3 : Week 12 (n=1)	261200			
Subject 3 : Week 24 (n=1)	57600			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Survived During the Study

End point title	Number of Subjects who Survived During the Study

End point description:

In this endpoint, number of subjects who survived during the study were observed. FAS included subjects who were assigned to investigational product and who took at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Screening (up to 28 days prior to Day 1 of treatment) up to 24 weeks of follow-up (approximately up to 28 weeks)

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Transfusion Independence at Weeks 12 and 24

End point title	Number of Subjects With Transfusion Independence at Weeks 12 and 24

End point description:

Transfusion independence at Week 12 was defined as when subjects did not have any transfusion records from the time of the first dose of the investigational product at Day 1 to the day of Week 12 visit (inclusive). Transfusion independence at Week 24 was defined as when subjects did not have any transfusion records from the day after Week 12 visit to the day of Week 24 visit (inclusive). FAS included subjects who were assigned to investigational product and who took at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Week 12 Transfusion Independence: Day 1 of Treatment up to Week 12 Follow-up Visit (approximately 12 weeks); Week 24 Transfusion Independence: Day after Week 12 Follow-up visit to Week 24 Follow-up Visit (approximately 12 weeks)

End point values	PF-06462700			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Week 12 Transfusion Independence	0			
Week 24 Transfusion Independence	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Screening up to 24 weeks of follow-up (approximately up to 28 weeks)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	PF-06462700

Reporting group description:

Subjects aged 2 years or >2 years with moderate and above severity aplastic anemia received PF-06462700 at a dose of 40 mg/kg/day, IV for 4 days. Subjects after treatment were followed up for 24 weeks.

Serious adverse events	PF-06462700		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	PF-06462700		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
General disorders and administration site conditions			
Infusion site extravasation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Feeling abnormal			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

Oedema subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Immune system disorders Serum sickness subjects affected / exposed occurrences (all) Hypogammaglobulinaemia subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1		
Reproductive system and breast disorders Genital haemorrhage subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood bilirubin increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) Blood lactate dehydrogenase increased	 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 		

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Lymphocyte count decreased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Oxygen saturation abnormal			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nervous system disorders			
Tremor			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Proctalgia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Nail bed inflammation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Acne			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Renal impairment			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Staphylococcal infection			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 2 2 / 3 (66.67%) 2		

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