Clinical trial results:
A Phase II Trial of R1507, a Recombinant Human Monoclonal Antibody to the Insulin-Like Growth Factor-1 Receptor for the Treatment of Patients with Recurrent or Refractory Ewing's Sarcoma, Osteosarcoma, Synovial Sarcoma, Rhabdomyosarcoma and Other Sarcomas

Summary

EudraCT number	2007-003940-30
Trial protocol	GB DE FR ES SE NL IT
Global end of trial date	19 February 2014

Results information

Result version number	v1 (current)
This version publication date	21 April 2016
First version publication date	21 April 2016

Trial information

Trial identification

Sponsor protocol code	NO21157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00642941
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	Final
Date of interim/final analysis	19 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 February 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study was primarily designed to determine objective response, progression-free survival (PFS), and the safety and tolerability of R1507 in participants with recurrent or refractory Ewing's sarcoma, osteosarcoma, synovial sarcoma, rhabdomyosarcoma and other sarcomas including alveolar soft part sarcoma, desmoplastic small round cell tumor, extraskeletal myxoid chondrosarcoma, clear cell sarcoma, and myxoid liposarcoma.

Protection of trial subjects:

The study was conducted in full conformance with the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever afforded greater protection to the participant. The study has fully adhered to the principles outlined in the Guideline for Good Clinical Practice (GCP) International Conference on Harmonisation (ICH) Tripartite Guideline (January 1997) or with local law if it afforded greater protection to the participant. For study sites in the European Union (EU)/European Economic Area (EEA), the study has also complied with the EU Clinical Trial Directive (2001/20/EC). For study sites in the United States (US) or under the US Investigational New Drug application (IND), the study has also adhered to the basic principles of GCP as outlined in the current version of 21 Code of Federal Regulations (CFR), subchapter D, part 312, “Responsibilities of Sponsors and Investigators”; part 50, “Protection of Human Subjects”; and part 56, “Institutional Review Boards”. In other countries where Guidelines for GCP exist, the Sponsor and the investigators have strictly ensured adherence to the stated provision.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	United States: 210
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Netherlands: 3

Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	317
EEA total number of subjects	93

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)	6
Adolescents (12-17 years)	54
Adults (18-64 years)	243
From 65 to 84 years	13
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A screening period was included prior to administration of study drug. Tumor scans/X-rays were to be obtained within 4 weeks, fluro-D-glucose positron emission tomography (FDG-PET) scans within 2 weeks, and Baseline laboratory evaluations within 1 week before first dose.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Ewing's Sarcoma Primary Cohort

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 milligrams per kilogram (mg/kg) via intravenous (IV) infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 1 included individuals with Ewing's sarcoma who had relapsed within 24 weeks after diagnosis and had received two or more prior chemotherapy regimens.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 2: Ewing's Sarcoma Secondary Cohort

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 2 included individuals with Ewing's sarcoma who had relapsed more than 24 weeks after diagnosis or had only received one prior chemotherapy regimen.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 3: Ewing's Sarcoma Expanded Cohort

Arm description:

Participants 2 to 21 years of age with recurrent or refractory sarcoma received R1507 as 27 mg/kg via IV infusion every 3 weeks until disease progression, intercurrent illness, unacceptable toxicity,

prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 3 included individuals with Ewing's sarcoma who were enrolled and treated following safety evaluation in other cohorts.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 4: Osteosarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 4 included individuals with osteosarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 5: Synovial Sarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 5 included individuals with synovial sarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 6: Rhabdomyosarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 6 included individuals with rhabdomyosarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 7a: Alveolar Soft Part Sarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7a included individuals with alveolar soft part sarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 7b: Desmoplastic Small Round Cell Tumors

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7b included individuals with desmoplastic small round cell tumors.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7c included individuals with extraskeletal myxoid chondrosarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 7d: Clear Cell Sarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity,

prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7d included individuals with clear cell sarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 7e: Myxoid Liposarcoma

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7e included individuals with myxoid liposarcoma.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Arm title	Cohort 8: Diagnosis Not Specified

Arm description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 8 included individuals with subtypes of sarcoma not specified in the protocol.

Arm type	Experimental
Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Investigational medicinal product name	R1507
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The drug product R1507 was reconstituted and administered via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks, depending upon the cohort in which the participant was enrolled.

Number of subjects in period 1	Cohort 1: Ewing's Sarcoma Primary Cohort	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort
Started	70	54	7
Completed	0	0	0
Not completed	70	54	7
Disease progression	60	50	5
Protocol violation	-	-	-
Death	4	-	1
Not specified	1	1	1
Refused treatment	1	-	-
Adverse event	1	1	-
Investigator decision	3	1	-
Study closed by Sponsor	-	1	-

Number of subjects in period 1	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma	Cohort 6: Rhabdomyosarcoma
Started	40	25	41
Completed	0	0	0
Not completed	40	25	41
Disease progression	36	23	39
Protocol violation	-	-	-
Death	1	2	1
Not specified	1	-	1
Refused treatment	2	-	-
Adverse event	-	-	-
Investigator decision	-	-	-
Study closed by Sponsor	-	-	-

Number of subjects in period 1	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Started	23	14	11
Completed	0	0	0
Not completed	23	14	11
Disease progression	18	12	10
Protocol violation	1	-	-
Death	-	-	-
Not specified	-	1	-
Refused treatment	2	-	1
Adverse event	1	1	-
Investigator decision	1	-	-
Study closed by Sponsor	-	-	-

Number of subjects in period 1	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified
Started	9	12	11
Completed	0	0	0
Not completed	9	12	11
Disease progression	7	12	7
Protocol violation	-	-	-
Death	-	-	1
Not specified	-	-	1
Refused treatment	-	-	1
Adverse event	1	-	-
Investigator decision	1	-	1
Study closed by Sponsor	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Ewing's Sarcoma Primary Cohort

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 milligrams per kilogram (mg/kg) via intravenous (IV) infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 1 included individuals with Ewing's sarcoma who had relapsed within 24 weeks after diagnosis and had received two or more prior chemotherapy regimens.

Reporting group title	Cohort 2: Ewing's Sarcoma Secondary Cohort

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 2 included individuals with Ewing's sarcoma who had relapsed more than 24 weeks after diagnosis or had only received one prior chemotherapy regimen.

Reporting group title	Cohort 3: Ewing's Sarcoma Expanded Cohort

Reporting group description:

Participants 2 to 21 years of age with recurrent or refractory sarcoma received R1507 as 27 mg/kg via IV infusion every 3 weeks until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 3 included individuals with Ewing's sarcoma who were enrolled and treated following safety evaluation in other cohorts.

Reporting group title	Cohort 4: Osteosarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 4 included individuals with osteosarcoma.

Reporting group title	Cohort 5: Synovial Sarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 5 included individuals with synovial sarcoma.

Reporting group title	Cohort 6: Rhabdomyosarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 6 included individuals with rhabdomyosarcoma.

Reporting group title	Cohort 7a: Alveolar Soft Part Sarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7a included individuals with alveolar soft part sarcoma.

Reporting group title	Cohort 7b: Desmoplastic Small Round Cell Tumors

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7b included individuals with desmoplastic small round cell tumors.

Reporting group title	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death.

Cohort 7c included individuals with extraskeletal myxoid chondrosarcoma.

Reporting group title	Cohort 7d: Clear Cell Sarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7d included individuals with clear cell sarcoma.

Reporting group title	Cohort 7e: Myxoid Liposarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7e included individuals with myxoid liposarcoma.

Reporting group title	Cohort 8: Diagnosis Not Specified

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 8 included individuals with subtypes of sarcoma not specified in the protocol.

Reporting group values	Cohort 1: Ewing's Sarcoma Primary Cohort	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort
Number of subjects	70	54	7
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	27	28.3	13.3
standard deviation	± 10.72	± 12.29	± 3.15
Gender categorical Units: Subjects			
Female	20	22	3
Male	50	32	4

Reporting group values	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma	Cohort 6: Rhabdomyosarcoma
Number of subjects	40	25	41
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	33.8	41.7	26.5
standard deviation	± 18.83	± 16.11	± 12.21
Gender categorical Units: Subjects			
Female	20	11	18
Male	20	14	23

Reporting group values	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma

Number of subjects	23	14	11
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	31.7	23.1	60.9
standard deviation	± 13.67	± 6.09	± 11.27
Gender categorical Units: Subjects			
Female	12	1	3
Male	11	13	8

Reporting group values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified
Number of subjects	9	12	11
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	26.9	50.6	30.7
standard deviation	± 11.01	± 11.06	± 18.56
Gender categorical Units: Subjects			
Female	2	3	3
Male	7	9	8

Reporting group values	Total		
Number of subjects	317		
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	118		
Male	199		

End points

End points reporting groups

Reporting group title	Cohort 1: Ewing's Sarcoma Primary Cohort

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 milligrams per kilogram (mg/kg) via intravenous (IV) infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 1 included individuals with Ewing's sarcoma who had relapsed within 24 weeks after diagnosis and had received two or more prior chemotherapy regimens.

Reporting group title	Cohort 2: Ewing's Sarcoma Secondary Cohort

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 2 included individuals with Ewing's sarcoma who had relapsed more than 24 weeks after diagnosis or had only received one prior chemotherapy regimen.

Reporting group title	Cohort 3: Ewing's Sarcoma Expanded Cohort

Reporting group description:

Participants 2 to 21 years of age with recurrent or refractory sarcoma received R1507 as 27 mg/kg via IV infusion every 3 weeks until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 3 included individuals with Ewing's sarcoma who were enrolled and treated following safety evaluation in other cohorts.

Reporting group title	Cohort 4: Osteosarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 4 included individuals with osteosarcoma.

Reporting group title	Cohort 5: Synovial Sarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 5 included individuals with synovial sarcoma.

Reporting group title	Cohort 6: Rhabdomyosarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 6 included individuals with rhabdomyosarcoma.

Reporting group title	Cohort 7a: Alveolar Soft Part Sarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7a included individuals with alveolar soft part sarcoma.

Reporting group title	Cohort 7b: Desmoplastic Small Round Cell Tumors

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7b included individuals with desmoplastic small round cell tumors.

Reporting group title	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death.

Cohort 7c included individuals with extraskeletal myxoid chondrosarcoma.

Reporting group title	Cohort 7d: Clear Cell Sarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7d included individuals with clear cell sarcoma.

Reporting group title	Cohort 7e: Myxoid Liposarcoma

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 7e included individuals with myxoid liposarcoma.

Reporting group title	Cohort 8: Diagnosis Not Specified

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 as 9 mg/kg via IV infusion once weekly until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death. Cohort 8 included individuals with subtypes of sarcoma not specified in the protocol.

Primary: Percentage of Participants with Complete or Partial Response According to World Health Organization (WHO) Response Criteria in Cohorts 2 to 8

End point title	Percentage of Participants with Complete or Partial Response According to World Health Organization (WHO) Response Criteria in Cohorts 2 to 8[1][2]

End point description:

Participants were assessed for tumor response according to WHO 1979 criteria. Complete response was defined as disappearance of all known disease, confirmed on two consecutive visits less than (<) 4 weeks apart. Partial response was defined as greater than or equal to (≥) 50 percent (%) decrease in total tumor load on two consecutive visits <4 weeks apart. The percentage of participants with either complete or partial response at any time during the study was to be calculated. All Treated Population: All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

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: The data were not analyzed because the development program was terminated by the Sponsor.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[3]	0[4]	0[5]	0[6]
Units: percentage of participants				
number (not applicable)				

Notes:

[3] - The data were not analyzed because the development program was terminated by the Sponsor.

[4] - The data were not analyzed because the development program was terminated by the Sponsor.

[5] - The data were not analyzed because the development program was terminated by the Sponsor.
[6] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[7]	0[8]	0[9]	0[10]
Units: percentage of participants				
number (not applicable)				

Notes:
[7] - The data were not analyzed because the development program was terminated by the Sponsor.
[8] - The data were not analyzed because the development program was terminated by the Sponsor.
[9] - The data were not analyzed because the development program was terminated by the Sponsor.
[10] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: percentage of participants				
number (not applicable)				

Notes:
[11] - The data were not analyzed because the development program was terminated by the Sponsor.
[12] - The data were not analyzed because the development program was terminated by the Sponsor.
[13] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Primary: PFS According to WHO Response Criteria at 18 Weeks from Start of R1507 Treatment in Cohort 1

End point title	PFS According to WHO Response Criteria at 18 Weeks from Start of R1507 Treatment in Cohort 1[14][15]

End point description:

PFS was defined as the time from start of treatment until first observation of death or disease progression. Progression was defined according to WHO 1979 criteria as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of PFS at 18 weeks from start of treatment was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Primary

End point timeframe:

Baseline, every 6 weeks until disease progression (up to 18 weeks)

Notes:
[14] - 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: The data were not analyzed because the development program was terminated by the Sponsor.
[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[16] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) According to WHO Response Criteria in Cohorts 2 to 8

End point title	Duration of Response (DOR) According to WHO Response Criteria in Cohorts 2 to 8[17]

End point description:

DOR was defined as the time from first documented complete or partial response until disease progression. Tumor response was assessed according to WHO 1979 criteria. Complete response was defined as disappearance of all known disease, confirmed on two consecutive visits <4 weeks apart. Partial response was defined as ≥50% decrease in total tumor load on two consecutive visits <4 weeks apart. Progression was defined as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of DOR was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	0[19]	0[20]	0[21]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[18] - The data were not analyzed because the development program was terminated by the Sponsor.

[19] - The data were not analyzed because the development program was terminated by the Sponsor.

[20] - The data were not analyzed because the development program was terminated by the Sponsor.

[21] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[22]	0[23]	0[24]	0[25]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[22] - The data were not analyzed because the development program was terminated by the Sponsor.

[23] - The data were not analyzed because the development program was terminated by the Sponsor.

[24] - The data were not analyzed because the development program was terminated by the Sponsor.

[25] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[26]	0[27]	0[28]	
Units: months				
median (full range (min-max))	(to)	(to)	(to)	

Notes:

[26] - The data were not analyzed because the development program was terminated by the Sponsor.

[27] - The data were not analyzed because the development program was terminated by the Sponsor.

[28] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP) According to WHO Response Criteria in Cohorts 2 to 8

End point title	Time to Progression (TTP) According to WHO Response Criteria in Cohorts 2 to 8[29]

End point description:

TTP was defined as the time from start of treatment until disease progression. Progression was defined according to WHO 1979 criteria as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of TTP was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[30]	0[31]	0[32]	0[33]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[30] - The data were not analyzed because the development program was terminated by the Sponsor.

[31] - The data were not analyzed because the development program was terminated by the Sponsor.

[32] - The data were not analyzed because the development program was terminated by the Sponsor.

[33] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[34]	0[35]	0[36]	0[37]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[34] - The data were not analyzed because the development program was terminated by the Sponsor.

[35] - The data were not analyzed because the development program was terminated by the Sponsor.

[36] - The data were not analyzed because the development program was terminated by the Sponsor.

[37] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[38]	0[39]	0[40]	
Units: months				
median (full range (min-max))	(to)	(to)	(to)	

Notes:

[38] - The data were not analyzed because the development program was terminated by the Sponsor.

[39] - The data were not analyzed because the development program was terminated by the Sponsor.

[40] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Failure-Free Survival (FFS) According to WHO Response Criteria in Cohorts 2 to 8

End point title	Failure-Free Survival (FFS) According to WHO Response Criteria in Cohorts 2 to 8[41]

End point description:

Participants were followed for survival status from enrollment until withdrawal from study. FFS was defined as the time from start of treatment until first observation of death or withdrawal from treatment for any reason. The median duration of OS was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[42]	0[43]	0[44]	0[45]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[42] - The data were not analyzed because the development program was terminated by the Sponsor.

[43] - The data were not analyzed because the development program was terminated by the Sponsor.

[44] - The data were not analyzed because the development program was terminated by the Sponsor.

[45] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[46]	0[47]	0[48]	0[49]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[46] - The data were not analyzed because the development program was terminated by the Sponsor.

[47] - The data were not analyzed because the development program was terminated by the Sponsor.

[48] - The data were not analyzed because the development program was terminated by the Sponsor.

[49] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[50]	0[51]	0[52]	
Units: months				
median (full range (min-max))	(to)	(to)	(to)	

Notes:

[50] - The data were not analyzed because the development program was terminated by the Sponsor.

[51] - The data were not analyzed because the development program was terminated by the Sponsor.

[52] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in Cohorts 2 to 8

End point title	Overall Survival (OS) in Cohorts 2 to 8[53]

End point description:

Participants were followed for survival status from enrollment until withdrawal from study. OS was defined as the time from start of treatment until death. The median duration of OS was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Continuously during treatment, then every 12 weeks until withdrawn consent (up to 6 years)

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[54]	0[55]	0[56]	0[57]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[54] - The data were not analyzed because the development program was terminated by the Sponsor.

[55] - The data were not analyzed because the development program was terminated by the Sponsor.

[56] - The data were not analyzed because the development program was terminated by the Sponsor.

[57] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[58]	0[59]	0[60]	0[61]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[58] - The data were not analyzed because the development program was terminated by the Sponsor.

[59] - The data were not analyzed because the development program was terminated by the Sponsor.

[60] - The data were not analyzed because the development program was terminated by the Sponsor.

[61] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[62]	0[63]	0[64]	
Units: months				
median (full range (min-max))	(to)	(to)	(to)	

Notes:

[62] - The data were not analyzed because the development program was terminated by the Sponsor.

[63] - The data were not analyzed because the development program was terminated by the Sponsor.

[64] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS According to WHO Response Criteria at 18 Weeks from Start of R1507 Treatment in Cohorts 2 to 8

End point title	PFS According to WHO Response Criteria at 18 Weeks from Start of R1507 Treatment in Cohorts 2 to 8[65]

End point description:

PFS was defined as the time from start of treatment until first observation of death or disease progression. Progression was defined according to WHO 1979 criteria as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of PFS at 18 weeks from start of treatment was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks until disease progression (up to 18 weeks)

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[66]	0[67]	0[68]	0[69]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[66] - The data were not analyzed because the development program was terminated by the Sponsor.

[67] - The data were not analyzed because the development program was terminated by the Sponsor.

[68] - The data were not analyzed because the development program was terminated by the Sponsor.

[69] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[70]	0[71]	0[72]	0[73]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[70] - The data were not analyzed because the development program was terminated by the Sponsor.

[71] - The data were not analyzed because the development program was terminated by the Sponsor.

[72] - The data were not analyzed because the development program was terminated by the Sponsor.

[73] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[74]	0[75]	0[76]	
Units: months				
median (full range (min-max))	(to)	(to)	(to)	

Notes:

[74] - The data were not analyzed because the development program was terminated by the Sponsor.

[75] - The data were not analyzed because the development program was terminated by the Sponsor.

[76] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS According to WHO Response Criteria in Cohorts 2 to 8

End point title	PFS According to WHO Response Criteria in Cohorts 2 to 8[77]

End point description:

PFS was defined as the time from start of treatment until first observation of death or disease progression. Progression was defined according to WHO 1979 criteria as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of PFS was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohort 1 are presented as a separate endpoint.

End point values	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma	Cohort 5: Synovial Sarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[78]	0[79]	0[80]	0[81]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[78] - The data were not analyzed because the development program was terminated by the Sponsor.

[79] - The data were not analyzed because the development program was terminated by the Sponsor.

[80] - The data were not analyzed because the development program was terminated by the Sponsor.

[81] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[82]	0[83]	0[84]	0[85]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[82] - The data were not analyzed because the development program was terminated by the Sponsor.

[83] - The data were not analyzed because the development program was terminated by the Sponsor.

[84] - The data were not analyzed because the development program was terminated by the Sponsor.

[85] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[86]	0[87]	0[88]	
Units: months				

median (full range (min-max))	(to)	(to)	(to)	

Notes:

[86] - The data were not analyzed because the development program was terminated by the Sponsor.

[87] - The data were not analyzed because the development program was terminated by the Sponsor.

[88] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Complete or Partial Response According to WHO Response Criteria in Cohort 1

End point title	Percentage of Participants with Complete or Partial Response According to WHO Response Criteria in Cohort 1[89]

End point description:

Participants were assessed for tumor response according to WHO 1979 criteria. Complete response was defined as disappearance of all known disease, confirmed on two consecutive visits <4 weeks apart. Partial response was defined as ≥50% decrease in total tumor load on two consecutive visits <4 weeks apart. The percentage of participants with either complete or partial response at any time during the study was calculated. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[89] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[90]			
Units: percentage of participants				
number (not applicable)				

Notes:

[90] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: TTP According to WHO Response Criteria in Cohort 1

End point title	TTP According to WHO Response Criteria in Cohort 1[91]

End point description:

TTP was defined as the time from start of treatment until disease progression. Progression was defined according to WHO 1979 criteria as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of TTP was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[91] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[92]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[92] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: FFS According to WHO Response Criteria in Cohort 1

End point title	FFS According to WHO Response Criteria in Cohort 1[93]

End point description:

Participants were followed for survival status from enrollment until withdrawal from study. FFS was defined as the time from start of treatment until first observation of death or withdrawal from treatment for any reason. The median duration of OS was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[93] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[94]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[94] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR According to WHO Response Criteria in Cohort 1

End point title	DOR According to WHO Response Criteria in Cohort 1[95]

End point description:

DOR was defined as the time from first documented complete or partial response until disease progression. Tumor response was assessed according to WHO 1979 criteria. Complete response was defined as disappearance of all known disease, confirmed on two consecutive visits <4 weeks apart. Partial response was defined as ≥50% decrease in total tumor load on two consecutive visits <4 weeks apart. Progression was defined as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of DOR was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[95] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[96]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[96] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS According to WHO Response Criteria in Cohort 1

End point title	PFS According to WHO Response Criteria in Cohort 1[97]

End point description:

PFS was defined as the time from start of treatment until first observation of death or disease progression. Progression was defined according to WHO 1979 criteria as ≥25% increase in area of one or more lesions, or the appearance of new lesions. The median duration of PFS was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Baseline, every 6 weeks for 24 weeks, then every 12 weeks until disease progression (up to 6 years)

Notes:

[97] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[98]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[98] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: OS in Cohort 1

End point title	OS in Cohort 1[99]

End point description:

Participants were followed for survival status from enrollment until withdrawal from study. OS was defined as the time from start of treatment until death. The median duration of OS was to be estimated using Kaplan-Meier methodology. All Treated Population.

End point type	Secondary

End point timeframe:

Continuously during treatment, then every 12 weeks until withdrawn consent (up to 6 years)

Notes:

[99] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Cohorts 2 to 8 are presented as a separate endpoint.

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort			
Subject group type	Reporting group			
Number of subjects analysed	0[100]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[100] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve of R1507

End point title	Area Under the Concentration-Time Curve of R1507

End point description:

Serum samples were obtained at various timepoints to assessed the pharmacokinetic profile of R1507. (The Ewing's Sarcoma Expanded Cohort provided additional samples in Weeks 3, 7, 10, and up to 30 days after last dose. Additionally, sampling was optional for participants <18 years of age.) The area under the concentration-time curve was to be calculated and averaged among all participants and expressed in hours by micrograms per milliliter (h*µg/mL). All Treated Population.

End point type	Secondary

End point timeframe:

Pre-dose (0 hours [h]), end of infusion (EOI), post-dose (2, 24, 72-96 h) in Week 1; pre-dose (0 h) and EOI in Weeks 2, 4, 6, 9; pre-dose (0 h), EOI, post-dose (48 h) in Week 12; pre-dose (0 h) in Week 13, and at time of final visit (up to 6 years)

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[101]	0[102]	0[103]	0[104]
Units: h*µg/mL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[101] - The data were not analyzed because the development program was terminated by the Sponsor.

[102] - The data were not analyzed because the development program was terminated by the Sponsor.

[103] - The data were not analyzed because the development program was terminated by the Sponsor.

[104] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 5: Synovial Sarcoma	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[105]	0[106]	0[107]	0[108]
Units: h*µg/mL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[105] - The data were not analyzed because the development program was terminated by the Sponsor.

[106] - The data were not analyzed because the development program was terminated by the Sponsor.

[107] - The data were not analyzed because the development program was terminated by the Sponsor.

[108] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[109]	0[110]	0[111]	0[112]
Units: h*µg/mL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[109] - The data were not analyzed because the development program was terminated by the Sponsor.

[110] - The data were not analyzed because the development program was terminated by the Sponsor.

[111] - The data were not analyzed because the development program was terminated by the Sponsor.

[112] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance of R1507

End point title	Clearance of R1507

End point description:

Serum samples were obtained at various timepoints to assessed the pharmacokinetic profile of R1507. (The Ewing's Sarcoma Expanded Cohort provided additional samples in Weeks 3, 7, 10, and up to 30 days after last dose. Additionally, sampling was optional for participants <18 years of age.) The maximum observed concentration across all observations was to be averaged among all participants. All Treated Population.

End point type	Secondary

End point timeframe:

Pre-dose (0 h), EOI, post-dose (2, 24, 72-96 h) in Week 1; pre-dose (0 h) and EOI in Weeks 2, 4, 6, 9; pre-dose (0 h), EOI, post-dose (48 h) in Week 12; pre-dose (0 h) in Week 13, and at time of final visit (up to 6 years)

End point values	Cohort 1: Ewing's Sarcoma Primary Cohort	Cohort 2: Ewing's Sarcoma Secondary Cohort	Cohort 3: Ewing's Sarcoma Expanded Cohort	Cohort 4: Osteosarcoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[113]	0[114]	0[115]	0[116]
Units: mL/day				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[113] - The data were not analyzed because the development program was terminated by the Sponsor.

[114] - The data were not analyzed because the development program was terminated by the Sponsor.

[115] - The data were not analyzed because the development program was terminated by the Sponsor.

[116] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 5: Synovial Sarcoma	Cohort 6: Rhabdomyosarcoma	Cohort 7a: Alveolar Soft Part Sarcoma	Cohort 7b: Desmoplastic Small Round Cell Tumors
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[117]	0[118]	0[119]	0[120]
Units: mL/day				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[117] - The data were not analyzed because the development program was terminated by the Sponsor.

[118] - The data were not analyzed because the development program was terminated by the Sponsor.

[119] - The data were not analyzed because the development program was terminated by the Sponsor.

[120] - The data were not analyzed because the development program was terminated by the Sponsor.

End point values	Cohort 7c: Extraskeletal Myxoid Chondrosarcoma	Cohort 7d: Clear Cell Sarcoma	Cohort 7e: Myxoid Liposarcoma	Cohort 8: Diagnosis Not Specified
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[121]	0[122]	0[123]	0[124]
Units: mL/day				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[121] - The data were not analyzed because the development program was terminated by the Sponsor.

[122] - The data were not analyzed because the development program was terminated by the Sponsor.

[123] - The data were not analyzed because the development program was terminated by the Sponsor.
[124] - The data were not analyzed because the development program was terminated by the Sponsor.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Continuously during treatment and approximately 7 days after discontinuation (up to 24 weeks)

Adverse event reporting additional description:

Safety Population: All participants who received at least one dose of study drug at had at least one safety follow-up assessment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	All Cohorts

Reporting group description:

Participants 2 years of age and older with recurrent or refractory sarcoma received R1507 via IV infusion as 9 mg/kg once weekly or 27 mg/kg every 3 weeks until disease progression, intercurrent illness, unacceptable toxicity, prolonged (2-week) time off treatment, withdrawal, loss to follow-up, investigator decision, or death.

Serious adverse events	All Cohorts		
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 317 (15.46%)		
number of deaths (all causes)	34		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			

subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Inflammation			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Dyspnoea			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Pneumothorax			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Spinal compression fracture			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders			
Facial palsy			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Somnolence			
subjects affected / exposed	3 / 317 (0.95%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Obstruction gastric			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 317 (0.63%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Hydronephrosis				
subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal haemorrhage				
subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 317 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Bacteraemia			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	3 / 317 (0.95%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			

subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 317 (0.63%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 317 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All Cohorts		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	277 / 317 (87.38%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	26 / 317 (8.20%)		
occurrences (all)	36		
Aspartate aminotransferase increased			
subjects affected / exposed	32 / 317 (10.09%)		
occurrences (all)	46		
Blood alkaline phosphatase increased			

subjects affected / exposed	22 / 317 (6.94%)		
occurrences (all)	24		
Blood lactate dehydrogenase increased			
subjects affected / exposed	17 / 317 (5.36%)		
occurrences (all)	17		
Weight decreased			
subjects affected / exposed	37 / 317 (11.67%)		
occurrences (all)	37		
Nervous system disorders			
Headache			
subjects affected / exposed	53 / 317 (16.72%)		
occurrences (all)	80		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	31 / 317 (9.78%)		
occurrences (all)	39		
Thrombocytopenia			
subjects affected / exposed	20 / 317 (6.31%)		
occurrences (all)	26		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	27 / 317 (8.52%)		
occurrences (all)	40		
Chest pain			
subjects affected / exposed	30 / 317 (9.46%)		
occurrences (all)	40		
Fatigue			
subjects affected / exposed	100 / 317 (31.55%)		
occurrences (all)	121		
Infusion related reaction			
subjects affected / exposed	18 / 317 (5.68%)		
occurrences (all)	22		
Pain			
subjects affected / exposed	28 / 317 (8.83%)		
occurrences (all)	39		
Pyrexia			

subjects affected / exposed	41 / 317 (12.93%)		
occurrences (all)	52		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	21 / 317 (6.62%)		
occurrences (all)	26		
Constipation			
subjects affected / exposed	49 / 317 (15.46%)		
occurrences (all)	53		
Diarrhoea			
subjects affected / exposed	56 / 317 (17.67%)		
occurrences (all)	99		
Nausea			
subjects affected / exposed	70 / 317 (22.08%)		
occurrences (all)	104		
Vomiting			
subjects affected / exposed	55 / 317 (17.35%)		
occurrences (all)	86		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	51 / 317 (16.09%)		
occurrences (all)	62		
Dyspnoea			
subjects affected / exposed	38 / 317 (11.99%)		
occurrences (all)	41		
Epistaxis			
subjects affected / exposed	21 / 317 (6.62%)		
occurrences (all)	25		
Oropharyngeal pain			
subjects affected / exposed	20 / 317 (6.31%)		
occurrences (all)	30		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	18 / 317 (5.68%)		
occurrences (all)	18		
Psychiatric disorders			

Anxiety			
subjects affected / exposed	22 / 317 (6.94%)		
occurrences (all)	22		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 317 (7.57%)		
occurrences (all)	29		
Back pain			
subjects affected / exposed	37 / 317 (11.67%)		
occurrences (all)	51		
Muscle spasms			
subjects affected / exposed	43 / 317 (13.56%)		
occurrences (all)	53		
Musculoskeletal pain			
subjects affected / exposed	27 / 317 (8.52%)		
occurrences (all)	30		
Pain in extremity			
subjects affected / exposed	24 / 317 (7.57%)		
occurrences (all)	29		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	47 / 317 (14.83%)		
occurrences (all)	53		
Hyperglycaemia			
subjects affected / exposed	48 / 317 (15.14%)		
occurrences (all)	76		
Hypoalbuminaemia			
subjects affected / exposed	18 / 317 (5.68%)		
occurrences (all)	21		
Hypokalaemia			
subjects affected / exposed	18 / 317 (5.68%)		
occurrences (all)	24		
Hyponatraemia			
subjects affected / exposed	22 / 317 (6.94%)		
occurrences (all)	25		
Hypophosphataemia			

subjects affected / exposed occurrences (all)	18 / 317 (5.68%) 21		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2007	The protocol was amended for administrative changes and minor clarifications, as well as updates to the timing of assessments. Blood sampling was made optional for participants <18 years of age. A statistical analysis plan was also added for pharmacokinetic endpoints.
01 August 2008	The protocol amendment was released to clarify the cohorts/study design, including the planned interim analysis for the Ewing's Sarcoma Primary Cohort. Secondary endpoints for TTP, FFS, and OS were also added. The minimum eligible age was changed from 12 years to 2 years. Among several other clarifications and formatting updates, the infusion time of R1507 was specified.
09 July 2009	The final protocol amendment added the Ewing's Sarcoma Expanded Cohort to allow testing of R1507 in a 3-week dosing schedule. Additional updates were made to accommodate the new cohort, including a special pharmacokinetic sampling schedule. The post-infusion monitoring time was also shortened on the basis of favorable tolerability in other clinical studies of R1507.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 February 2014	The last dose of study drug was received, after which the study was closed by the Sponsor on the basis of decisions to discontinue further development of R1507. The decision was not due to safety concerns.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was closed to further enrollment due to a decision by the Sponsor to discontinue development of R1507. The decision was made based upon available data from other completed/ongoing trials of R1507 and was not due to safety concerns.

Notes: