



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

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|--|----|
| 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, fluoro-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: Extraskelatal 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 standard deviation | 27 ± 10.72 | 28.3 ± 12.29 | 13.3 ± 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 standard deviation | 33.8 ± 18.83 | 41.7 ± 16.11 | 26.5 ± 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 $\geq 25\%$ 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 $\geq 25\%$ 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: Extraskelatal 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 $\geq 25\%$ 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 $\geq 25\%$ 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 $\geq 50\%$ 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 $\geq 25\%$ 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 $\geq 50\%$ decrease in total tumor load on two consecutive visits <4 weeks apart. Progression was defined as $\geq 25\%$ 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 $\geq 25\%$ 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 occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 317 (0.63%) 0 / 2 0 / 1 | | |
| Bacteraemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 317 (0.32%) 0 / 1 0 / 0 | | |
| Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 317 (0.32%) 0 / 1 0 / 0 | | |
| Device related infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 317 (0.63%) 0 / 2 0 / 0 | | |
| Escherichia sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 317 (0.32%) 0 / 1 0 / 0 | | |
| Infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 317 (0.95%) 0 / 3 0 / 0 | | |
| Pyelonephritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 317 (0.32%) 0 / 1 0 / 0 | | |
| Sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 317 (0.32%) 0 / 2 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 occurrences (all) | 22 / 317 (6.94%) 22 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 24 / 317 (7.57%) 29 | | |
| Back pain subjects affected / exposed occurrences (all) | 37 / 317 (11.67%) 51 | | |
| Muscle spasms subjects affected / exposed occurrences (all) | 43 / 317 (13.56%) 53 | | |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 27 / 317 (8.52%) 30 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 24 / 317 (7.57%) 29 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 47 / 317 (14.83%) 53 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 48 / 317 (15.14%) 76 | | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 18 / 317 (5.68%) 21 | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 18 / 317 (5.68%) 24 | | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 22 / 317 (6.94%) 25 | | |
| Hypophosphataemia | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 18 / 317 (5.68%) | | |
| occurrences (all) | 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: