



Clinical trial results: Efficacy of Olaratumab and Rechallenge with Doxorubicin in anthracycline pretreated, advanced soft tissue sarcoma patients. An exploratory phase-II study - The OlaReDo Phase II Trial

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-001124-20 |
| Trial protocol | DE |
| Global end of trial date | 25 June 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 04 November 2021 |
| First version publication date | 04 November 2021 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | GISG-17 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03698227 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest |
| Sponsor organisation address | Steinbacher Hohl 2-26, Frankfurt, Germany, 60488 |
| Public contact | IKF, Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest, 0049 6976014420, olaredo@ikf-khnw.de |
| Scientific contact | IKF, Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest, 0049 6976014420, olaredo@ikf-khnw.de |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 17 May 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 June 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 June 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The present study aimed to evaluate efficacy and safety of olaratumab and doxorubicin combined with the cardioprotective prophylaxis with dexrazoxane in anthracycline pretreated patients. Efficacy was addressed by the progression-free survival rate after 3 months (PFSR3), assessed by applying RECIST 1.1, as primary endpoint and PFS, objective response rate, disease control rate and overall survival as secondary endpoints.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and the trial was approved by an Independent Ethics Committee. The eligibility of a new patient was determined by the local investigator during regular clinical visits. The examinations for the study and the inclusion of the patient were done after detailed written and oral education by use of the informed consent forms and after given written consent of the patient.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 14 November 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Germany: 2 |
| Worldwide total number of subjects | 2 |
| EEA total number of subjects | 2 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 2 |

| | |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Based on the negative results (lack of efficacy) on olaratumab in the ANNOUNCE study (press release dated January 18th, 2019), recruitment of the OlaReDo study was stopped immediately and the so far two enrolled patients were informed by the investigators accordingly.

Pre-assignment

Screening details:

Study was prematurely stopped after enrollment of 2 patients

Period 1

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

Arms

| | |
|-----------|-------|
| Arm title | Arm A |
|-----------|-------|

Arm description:

patients received 8 cycles (q3w) of olaratumab administered IV (20 mg/kg on day 1 and day 8 of cycle 1 and 15 mg/kg on day 1 and day 8 of cycle 2 to 8) combined with doxorubicin administered IV (75 mg/m² on day 1 of each cycle for 8 cycles) and dexrazoxane administered IV (at a dose equal to 10 times the doxorubicin dose [mg/m²] on day 1 of each cycle for 8 cycles). According to the study protocol, beginning with cycle 9 Olaratumab maintenance monotherapy should have been performed at 15 mg/kg administered IV on day 1 and day 8 of each subsequent 21 day cycle until documented progressive disease (PD), unacceptable toxicity, or other discontinuation criteria are met. However, due to negative results (lack of efficacy) on olaratumab in the ANNOUNCE study, treatment in the maintenance phase was not performed.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Olaratumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for concentrate for solution for infusion |
| Routes of administration | Infusion , Injection |

Dosage and administration details:

olaratumab was administered IV; 20 mg/kg on day 1 and day 8 of cycle 1 and 15 mg/kg on day 1 and day 8 of cycle 2 to 8

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Infusion |

Dosage and administration details:

doxorubicin was administered IV; 75 mg/m² on day 1 of each cycle for 8 cycles

| | |
|--|---|
| Investigational medicinal product name | Dexrazoxane |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for concentrate for solution for infusion |
| Routes of administration | Infusion |

Dosage and administration details:

dexrazoxane was administered IV at a dose equal to 10 times the doxorubicin dose [mg/m²] on day 1 of each cycle for 8 cycles

| Number of subjects in period 1 | Arm A |
|---------------------------------------|-------|
| Started | 2 |
| Completed | 2 |

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---------------------------------------|---------------|-------|--|
| Number of subjects | 2 | 2 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 2 | 2 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | 1 | |
| Male | 1 | 1 | |
| type of tumor | | | |
| Units: Subjects | | | |
| Chondrosarcoma, upper extremity | 1 | 1 | |
| Synovial sarcoma, trunk | 1 | 1 | |
| ECOG Performance Status | | | |
| Units: Subjects | | | |
| ECOG 0 | 1 | 1 | |
| ECOG 1 | 1 | 1 | |
| TNM stage and histopathological grade | | | |
| Units: Subjects | | | |
| unknown | 1 | 1 | |
| T/N - not documented; M0; G3 | 1 | 1 | |
| AJCC stage at study entry | | | |
| Units: Subjects | | | |
| IV | 1 | 1 | |
| unknown | 1 | 1 | |

End points

End points reporting groups

| | |
|--|-------|
| Reporting group title | Arm A |
| Reporting group description: patients received 8 cycles (q3w) of olaratumab administered IV (20 mg/kg on day 1 and day 8 of cycle 1 and 15 mg/kg on day 1 and day 8 of cycle 2 to 8) combined with doxorubicin administered IV (75 mg/m ² on day 1 of each cycle for 8 cycles) and dexrazoxane administered IV (at a dose equal to 10 times the doxorubicin dose [mg/m ²] on day 1 of each cycle for 8 cycles). According to the study protocol, beginning with cycle 9 Olaratumab maintenance monotherapy should have been performed at 15 mg/kg administered IV on day 1 and day 8 of each subsequent 21 day cycle until documented progressive disease (PD), unacceptable toxicity, or other discontinuation criteria are met. However, due to negative results (lack of efficacy) on olaratumab in the ANNOUNCE study, treatment in the maintenance phase was not performed. | |

Primary: Progression Free survival after 3 months PFSR3

| | |
|--|---|
| End point title | Progression Free survival after 3 months PFSR3 ^[1] |
| End point description: Due to the small sample size of only two patients, it was not possible to perform statistical analyses with aggregated data. Thus, only data listings by individual patient have been provided. Out of two enrolled patients, both patients showed progressive-free survival after 3 months of study treatment | |
| End point type | Primary |
| End point timeframe: tumor response was determined radiologically prior every second combination treatment cycle (approx. every 6 weeks \pm 7 days), during follow up tumor assessment was performed every 3 months \pm 3 weeks | |
| 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: Due to sample size of only 2 patients no statistical analyses were possible | |

| End point values | Arm A | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Subjects | | | | |
| YES | 2 | | | |
| NO | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

| | |
|---|---------------------------|
| End point title | Progression-free survival |
| End point description: Progression-free survival (PFS) was defined as the time from the first dosing date of any study medication to the date of the first objectively documented tumor progression, or death due to any cause | |
| End point type | Secondary |

End point timeframe:

eventual signs of progressive disease and death events were to be assessed and recorded during trial participation (i.e. study drug medication) and the follow-up period which was 6 months

| End point values | Arm A | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Subjects | | | | |
| No Progression | 1 | | | |
| Progression | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|-----------------|------------------|
| End point title | Overall survival |
|-----------------|------------------|

End point description:

Overall survival (OS) was defined as the time from date of the first dosing date of any study medication to the date of death (due to any cause). Subjects who are alive were censored at the last known alive dates

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

eventual signs of progressive disease and death events were to be assessed and recorded during trial participation (i.e. study drug medication) and the follow-up period which was 6 months

| End point values | Arm A | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Subjects | | | | |
| No Death | 2 | | | |
| Death | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Best overall response

| | |
|-----------------|-----------------------|
| End point title | Best overall response |
|-----------------|-----------------------|

End point description:

both patients revealed detectable tumor lesions and valid restaging data for applying RECIST 1.1 criteria. Out of these, 1 patient showed stable disease (SD) until end of study (EOS), the other patient

showed stable disease (SD) until the cycle 8 and revealed progressive disease (PD) thereafter

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

tumor response was determined radiologically prior every second combination treatment cycle (approx. every 6 weeks \pm 7 days). During follow up (until disease progression of EOS) tumor assessment was performed every 3 months \pm 3 weeks

| End point values | Arm A | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Subjects | | | | |
| Stable disease | 1 | | | |
| progressive disease | 1 | | | |
| complete response | 0 | | | |
| partial response | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed continuously during the study (signature of the informed consent form - up to 30 days after last administration IMP). Thereafter, only SAEs at least possibly related to study treatment were reported

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 22 |

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Arm A |
|-----------------------|-------|

Reporting group description:

patients received 8 cycles (q3w) of olaratumab administered IV (20 mg/kg on day 1 and day 8 of cycle 1 and 15 mg/kg on day 1 and day 8 of cycle 2 to 8) combined with doxorubicin administered IV (75 mg/m² on day 1 of each cycle for 8 cycles) and dexrazoxane administered IV (at a dose equal to 10 times the doxorubicin dose [mg/m²] on day 1 of each cycle for 8 cycles). According to the study protocol, beginning with cycle 9 Olaratumab maintenance monotherapy should have been performed at 15 mg/kg administered IV on day 1 and day 8 of each subsequent 21 day cycle until documented progressive disease (PD), unacceptable toxicity, or other discontinuation criteria are met. However, due to negative results (lack of efficacy) on olaratumab in the ANNOUNCE study, treatment in the maintenance phase was not performed.

| Serious adverse events | Arm A | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| 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 | Arm A | | |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | | |
| Investigations | | | |
| Neutrophil count decreased | | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 5 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 10 | | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 14 | | |
| Cardiac disorders Cardiac disorder - anthracycline induced cardiomyopathy subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 2 / 2 (100.00%) 6 | | |
| Chills subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 3 | | |
| Edema limbs subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Constipation | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Mucositis oral | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 2 | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | | |
| occurrences (all) | 4 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-----------------|---|--------------|
| 18 January 2019 | Based on the negative results (lack of efficacy) on olaratumab in the ANNOUNCE study (press release dated January 18th, 2019), recruitment of the OlaReDo study was stopped immediately and the two enrolled patients were informed by the investigators accordingly. A halt of the OlaReDo study was notified by the Sponsor to the Competent Authority and Ethics Committee on January 22nd, 2019. Acknowledgement of receipt PEI: 28-Jan-2019; acknowledgement of receipt IRB: 25-Jan-2019 | - |

Notes:

Limitations and caveats

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

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|--|
| The OlaReDo study was stopped prematurely with only 2 patients treated according the study protocol. Due to the small sample size of only two patients, statistical analyses were not possible |
|--|

Notes: