



Clinical trial results: CDK4/6 inhibition in locally advanced/metastatic chordoma Summary

EudraCT number	2016-004660-19
Trial protocol	DE
Global end of trial date	22 December 2022

Results information

Result version number	v1 (current)
This version publication date	02 January 2026
First version publication date	02 January 2026

Trial information

Trial identification

Sponsor protocol code	NCT-2016-415
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03110744
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ruprecht-Karls-University Heidelberg, Medical Faculty
Sponsor organisation address	Im Neuenheimer Feld 672, Heidelberg, Germany, 69120
Public contact	NCT Trial Center, Heidelberg University Hospital, studienzentrale@nct-heidelberg.de
Scientific contact	NCT Trial Center, Heidelberg University Hospital, studienzentrale@nct-heidelberg.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	11 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2022
Global end of trial reached?	Yes
Global end of trial date	22 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective of this phase II trial is to gain first evidence of antitumor activity of palbociclib in adult patients with (locally) advanced or metastasized chordoma not amenable to curative treatment with surgery or radiotherapy.

Protection of trial subjects:

During and following a patient's participation in the trial, the investigator should ensure that adequate medical care was provided to a patient for any AE, including clinically significant laboratory values. The investigator should inform a patient when medical care was needed for intercurrent illness(es) of which the investigator becomes aware.

Background therapy:

not applicable

Evidence for comparator:

not applicable

Actual start date of recruitment	31 January 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: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	26

From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First enrollment (FPI): 31.01.2018

Last Enrollment (LPI): 28.04.2022

Pre-assignment

Screening details:

Screening period (Baseline visit): Day -28 to 0

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	Palbociclib
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Palbociclib (Ibrance®)
Investigational medicinal product code	PD-0332991-00
Other name	
Pharmaceutical forms	Capsule, hard + tablet
Routes of administration	Oral use

Dosage and administration details:

oral administration once per day for 21 days in a 28-day cycle

Number of subjects in period 1 ^[1]	Palbociclib
Started	28
Completed	28

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The given numbers cannot be adapted to the structure of the database.

Baseline characteristics

Reporting groups

Reporting group title	Palbociclib
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Reporting group description: -

Reporting group values	Palbociclib	Total	
Number of subjects	28	28	
Age categorical			
Units: Subjects			
18-44	3	3	
45-64	15	15	
>=65	10	10	
Age continuous			
Units: years			
arithmetic mean	58.9		
standard deviation	± 12.95	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	21	21	

Subject analysis sets

Subject analysis set title	full analysis set
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Subject analysis set type	Full analysis
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Subject analysis set description:

All enrolled patients who have finished at least one cycle of the study medication and who are evaluable for the primary endpoint are included in the full analysis set under the ITT principle.

The primary endpoint is the disease control rate (DCR) after six cycles of palbociclib, which is defined as the presence of complete response (CR) or partial response (PR) or stable disease (SD) according to RECIST version 1.1.

Subject analysis set title	safety analysis set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

All enrolled patients who have received any amount of the study medication are subject of the safety population.

Reporting group values	full analysis set	safety analysis set	
Number of subjects	25	28	
Age categorical			
Units: Subjects			
18-44	2	3	
45-64	13	15	
>=65	10	10	
Age continuous			
Units: years			
arithmetic mean	60.1	58.9	
standard deviation	± 12.32	± 12.95	

Gender categorical			
Units: Subjects			
Female	6	7	
Male	19	21	

End points

End points reporting groups

Reporting group title	Palbociclib
Reporting group description: -	
Subject analysis set title	full analysis set
Subject analysis set type	Full analysis
Subject analysis set description: All enrolled patients who have finished at least one cycle of the study medication and who are evaluable for the primary endpoint are included in the full analysis set under the ITT principle. The primary endpoint is the disease control rate (DCR) after six cycles of palbociclib, which is defined as the presence of complete response (CR) or partial response (PR) or stable disease (SD) according to RECIST version 1.1.	
Subject analysis set title	safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: All enrolled patients who have received any amount of the study medication are subject of the safety population.	

Primary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description: The primary endpoint is the disease control rate (DCR) after six cycles of palbociclib, which is defined as the presence of complete response (CR) or partial response (PR) or stable disease (SD) according to RECIST version 1.1.	
End point type	Primary
End point timeframe: From the six cycle of palbociclib to end of study.	

End point values	Palbociclib	full analysis set	safety analysis set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	25	28	
Units: rate				
number (confidence interval 95%)				
DCR	0.440 (0.244 to 0.651)	0.440 (0.244 to 0.651)	0.393 (0.215 to 0.594)	

Statistical analyses

Statistical analysis title	DCR analysis
Statistical analysis description: Null hypothesis: the true response rate p is less or equal to a reference rate p_0 is tested against a one-sided alternative, where p is the true response probability, p_0 , the (uninteresting) reference response rate, and p_1 the (desirable) target level. In the final analysis the null hypothesis is rejected and the drug recommended for further development if 8 or more responses are observed in 43 patients. This design yields a type I error rate of ≤ 0.05 and power of $\geq 80\%$ when $p=0.25$	
Comparison groups	Palbociclib v full analysis set v safety analysis set

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	≤ 0.05 ^[2]
Method	Ratio

Notes:

[1] - After 8 responders with stable disease (SD), it was decided to terminate the study as sufficient evidence was obtained to reject the null hypothesis. 42 patients were recruited and screened, of whom 28 started treatment with IMP.

[2] - This p-value was used for the sample size calculation and the primary endpoint analysis consisted on a rate.

Secondary: Tumor Response Rate (TRR)

End point title	Tumor Response Rate (TRR)
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End point description:

The TRR is defined as the sum of complete response (CR) and partial response (PR) according to RECIST version 1.1 after six cycles of study medication.

End point type	Secondary
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End point timeframe:

From the six cycle of palbociclib to end of study.

End point values	Palbociclib	full analysis set	safety analysis set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	25	28	
Units: Ratio				
number (not applicable)				
TRR	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)
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End point description:

PFS is defined as the time in months from first administration of the IMP to progression of disease or death from any cause, whichever occurs first. Patients without the event are censored on the last date of follow-up.

End point type	Secondary
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End point timeframe:

From first administration of the IMP to progression of disease or death from any cause, whichever occurs first (up to last patient last visit).

End point values	full analysis set	safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25 ^[3]	28 ^[4]		
Units: months				
number (not applicable)				
Kaplan Meier Analysis: 25% estimate	4.0	2.8		
Kaplan Meier Analysis: 50% estimate	5.8	5.6		
Kaplan Meier Analysis: 75% estimate	11.1	11.1		

Notes:

[3] - 18 patients with event

[4] - 20 patients with event

Attachments (see zip file)	PFS safety analysis set/5.3.2_Chordoma_timetoevent.pdf PFS full analysis set/5.3.1_Chordoma_timetoevent.pdf
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Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description: OS is defined as the time in months from first administration of the IMP to time of death from any cause. Patients without the event are censored on the last date of follow-up.	
End point type	Secondary
End point timeframe: From first administration of the IMP to time of death from any cause (up to last patient last visit).	

End point values	Palbociclib	full analysis set	safety analysis set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	28 ^[5]	25 ^[6]	28 ^[7]	
Units: months				
number (not applicable)				
Kaplan Meier Analysis: 25% estimate	10.8	13.8	10.8	
Kaplan Meier Analysis: 50% estimate	24.6	34.0	24.6	
Kaplan Meier Analysis: 75% estimate	50.1	50.1	50.1	

Notes:

[5] - 14 patients with event

[6] - 12 patients with event

[7] - 14 patients with event

Attachments (see zip file)	OS full analysis set/5.4.1_Chordoma_timetoevent.pdf OS safety analysis set/5.4.2_Chordoma_timetoevent.pdf
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Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In this trial, all AEs that occur after first administration of the IMP are documented. The individual period of observation ends 28 days after the last dose of the IMP for chordoma.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Safety population
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Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 28 (35.71%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to peritoneum			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Neoplasm progression			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
tumor pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Social stay hospitalisation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Catheterisation cardiac			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary arterial pressure increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Dislocation of vertebra			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoaesthesia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paralysis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Pancytopenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal perforation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Mechanical ileus			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteolysis			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Implant site infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Staphylococcal infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 28 (32.14%)		
occurrences (all)	9		
Leukopenia			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	7		
Neutropenia			
subjects affected / exposed	10 / 28 (35.71%)		
occurrences (all)	10		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	6 / 28 (21.43%)		
occurrences (all)	6		
Gait disturbance			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
General physical health deterioration			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Mucosal disorder			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pyrexia			

subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all) Vertigo positional subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Eye disorders Astigmatism subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Dysphagia	1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 2 / 28 (7.14%) 2 4 / 28 (14.29%) 4 1 / 28 (3.57%) 1		

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Gastritis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Lip dry			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	5		
Proctalgia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Endocrine disorders			

Hypothyroidism subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2018	Substantial Amendment 1
16 November 2020	Substantial Amendment 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported