Clinical trial results:
Early identification of patients who benefit from palbociclib in addition to letrozole

Summary

EudraCT number	2015-004231-12
Trial protocol	NL
Global end of trial date	28 September 2022

Results information

Result version number	v1 (current)
This version publication date	08 February 2023
First version publication date	08 February 2023

Trial information

Trial identification

Sponsor protocol code	NL20151001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02806050
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Groningen
Sponsor organisation address	Hanzeplein 1, Groningen, Netherlands, 9713 GZ
Public contact	CP Schröder, University Medical Center Groningen, +31 503616161, c.p.schroder@umcg.nl
Scientific contact	CP Schröder, University Medical Center Groningen, +31 503616161, c.p.schroder@umcg.nl

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	28 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 September 2022
Global end of trial reached?	Yes
Global end of trial date	28 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate in a feasibility study whether low uptake on FES-PET at baseline is related to non response to letrozole plus palbociclib treatment.

Protection of trial subjects:

All patients will receive an effective treatment combination. In addition to the standard control visits to the clinic, three extra visits will be performed as part of the study: for screening, for the FES-PET scan and for the early FDG-PET. The FESPET scan will induce an extra radiation burden of 6.1 mSv and the early FDG-PET 5 mSv. In the future, this study may potentially contribute to improved selection of patients for this combination treatment. This is of relevance in view of optimal treatment for individual patients, avoiding unnecessary toxicity and financial burden.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2016
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	Netherlands: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	20
From 65 to 84 years	9

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

31 patients were included in the study, 29 patients completed the study.
2 patients discontinued the study prematurely:
- 1 patient had dural metastases therefore no response PET/CT scan was performed
- 1 patient had elevated liver enzymes, therefore a response PET/CT was performed after 1 cycle (instead of after 2 cycles), progressive disease

Pre-assignment

Screening details:

See enclosed paper

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 and FES PET

Arm description:

To evaluate whether low uptake on FES-PET at baseline is related to non-response to letrozole plus palbociclib treatment.

Arm type	Experimental
Investigational medicinal product name	18F-FES
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

total 200 MBq

Investigational medicinal product name	Palbociclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

per day 125 mg

Number of subjects in period 1	Palbociclib and FES PET
Started	29
Completed	29

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	29	29	
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	
From 65-84 years	9	9	
Gender categorical Units: Subjects			
Female	29	29	
Male	0	0	

Subject analysis sets

Subject analysis set title	Palbociclib and FES PET
Subject analysis set type	Full analysis

Subject analysis set description:
study population

Reporting group values	Palbociclib and FES PET		
Number of subjects	29		
Age categorical Units: Subjects			
Adults (18-64 years)	20		
From 65-84 years	9		
Gender categorical Units: Subjects			
Female	29		
Male	0		

End points

End points reporting groups

Reporting group title	Palbociclib and FES PET
Reporting group description: To evaluate whether low uptake on FES-PET at baseline is related to non-response to letrozole plus palbociclib treatment.	
Subject analysis set title	Palbociclib and FES PET
Subject analysis set type	Full analysis
Subject analysis set description: study population	

Primary: The relation between low uptake on FES-PET to response per lesion

End point title	The relation between low uptake on FES-PET to response per lesion[1]
End point description:	
End point type	Primary
End point timeframe: 8 weeks after start of treatment	

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: See enclosed paper

End point values	Palbociclib and FES PET	Palbociclib and FES PET		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	29	29		
Units: SUV	29	29		

Statistical analyses

No statistical analyses for this end point

Secondary: quantitative FES-uptake and correlation with progression free survival

End point title	quantitative FES-uptake and correlation with progression free survival
End point description:	
End point type	Secondary
End point timeframe: 6 months	

End point values	Palbociclib and FES PET	Palbociclib and FES PET		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	29	29		
Units: SUV	29	29		

Statistical analyses

No statistical analyses for this end point

Secondary: analysis of circulating tumor DNA and correlation with FES-PET results and progression free survival

End point title	analysis of circulating tumor DNA and correlation with FES-PET results and progression free survival

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Palbociclib and FES PET	Palbociclib and FES PET		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	29	29		
Units: SUV	29	29		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
During the study	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

Frequency threshold for reporting non-serious adverse events: 3 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: See enclosed paper

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2017	1. Moving the FDG PET scan from 8 weeks to 2 weeks after the start of treatment. 2. Expand the number of patients from n=15 to n=30 for the implementation of point 1. Expanding the number of patients also enables further refinement of the FES-PET analysis: namely by adding a per-patient analysis with regard to response, in addition to the per-lesion analysis (the primary endpoint).
14 August 2017	update IMPD
12 February 2018	1. Expand inclusion of exclusively postmenopausal patients with also premenopausal patients, provided they are undergoing ovarian suppression with an LHRH analog 2. Textual adjustment in PIF and protocol that the combination treatment in The Netherlands is registered
21 August 2018	Diagnostic change in follow-up, in which the CT scan every 3 months for measurable disease according to RECIST criteria 1.1 is cancelled
18 September 2018	Update investigator's brochure palbociclib

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31891878