Clinical trial results:
Effect of the moderate CYP3A4-inhibitor erythromycin on the pharmacokinetics of palbociclib

Summary

EudraCT number	2018-004032-29
Trial protocol	NL
Global end of trial date	10 May 2021

Results information

Result version number	v1 (current)
This version publication date	24 July 2022
First version publication date	24 July 2022
Summary attachment (see zip file)	Publication CLINICAL PHARMACOLOGY & THERAPEUTICS: Effects of the Moderate CYP3A4 Inhibitor Erythromycin on the Pharmacokinetics of Palbociclib (PUblicatie M18CYP.pdf)

Trial information

Trial identification

Sponsor protocol code	M18CYP

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital
Sponsor organisation address	Plesmanlaan 121, Amsterdam, Netherlands,
Public contact	Neeltje Steeghs, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, n.steeghs@nki.nl
Scientific contact	Neeltje Steeghs, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, n.steeghs@nki.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	12 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 May 2021
Global end of trial reached?	Yes
Global end of trial date	10 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to study the effect of the moderate CYP3A4 inhibitor erythromycin on the pharmacokinetics of palbociclib, measured as AUC0-24h, Cmax and Cmin.

Protection of trial subjects:

Theoretically, the concomitant administration of palbociclib with erythromycin could lead to higher palbociclib exposure and thus give an increased risk of toxicities. However, the duration of this intervention is short (7 days). Although erythromycin rarely gives toxicities, this is a minor risk for patients. Since erythromycin could prolong the QTc interval, an ECG will be performed at screening. Patients with a prolonged QTc interval will be excluded.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	8
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with histological or cytological proof of cancer with an indicationfor treatment with palbociclib (i.e., advanced breast cancer) at the standard dose of 125 mg q.d. were eligible for inclusion. Further inclusion criteria were aged ≥18 years, World Health Organization performance status of 0, 1, or 2, and adequate organ function.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

start with either palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.) and then crossover to palbociclib monotherapy 125 mg q.d.

Arm type	Experimental
Investigational medicinal product name	palbociclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were randomized to start with either palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.) and then crossover to palbociclib monotherapy 125 mg q.d.

Investigational medicinal product name	Erythromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were randomized to start with either palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.) and then crossover to palbociclib monotherapy 125 mg q.d.

Arm title	Arm B

Arm description:

Start with palbociclib monotherapy 125 mg q.d. and then crossover to palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.)

Arm type	Experimental
Investigational medicinal product name	palbociclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Start with palbociclib monotherapy 125 mg q.d. and then crossover to palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.)

Investigational medicinal product name	Erythromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Start with palbociclib monotherapy 125 mg q.d. and then crossover to palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.)

Number of subjects in period 1	Arm A	Arm B
Started	6	6
Completed	6	5
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
start with either palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.) and then crossover to palbociclib monotherapy 125 mg q.d.	
Reporting group title	Arm B
Reporting group description:	
Start with palbociclib monotherapy 125 mg q.d. and then crossover to palbociclib 125 mg q.d. combined with erythromycin 500 mg three times daily (t.i.d.)	

Primary: Pharmacokinetics

End point title	Pharmacokinetics[1]
End point description:	
To study the effect of the moderate CYP3A4 inhibitor erythromycin on the pharmacokinetics of palbociclib, measured as AUC0-24h, Cmax and Cmin.	
End point type	Primary
End point timeframe:	
At Day 7 and Day 21 , patients were admitted and blood samples were collected for pharmacokinetic analyses. Timepoints were before dosing (directly before ingestion of palbociclib) and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 24 hrs post dosing	

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 table 2 of publication attached

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: ng/mL and ng*h/mL				
number (not applicable)	6	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events should be collected beginning from the time the patient starts the study treatment (Day 1) and ending with end of the study (Day 21).

Assessment type	Systematic

Dictionary used

Dictionary name	CTC
Dictionary version	5.0

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

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 table 3 of publication attached.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2019	Erasmus Medical Center added as trial center
08 December 2020	Change # evaluable patients to 11 patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported