Clinical trial results:
Fluconazole pharmacokinetics, including bioavailability, in Obese subjects after an Intravenous and oral Administration (FOLIA).

Summary

EudraCT number	2018-002613-35
Trial protocol	NL
Global end of trial date	21 March 2021

Results information

Result version number	v1 (current)
This version publication date	01 September 2023
First version publication date	01 September 2023

Trial information

Trial identification

Sponsor protocol code	UMCN-AKF-18.07

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboud UMC
Sponsor organisation address	Geert Grooteplein 10, Nijmegen, Netherlands,
Public contact	Roger Brüggemann, Radboud university medical center, +31 243616405, roger.bruggemann@radboudumc.nl
Scientific contact	Roger Brüggemann, Radboud university medical center, +31 243616405, roger.bruggemann@radboudumc.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	21 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2021
Global end of trial reached?	Yes
Global end of trial date	21 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of obesity (BMI ≥35 kg/m2) and bariatric surgery on the pharmacokinetics, including oral bioavailability of fluconazole.

Protection of trial subjects:

n.a.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 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: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

a. obese groups: subject must have a BMI ≥35 kg/m2 at the time of inclusion or has undergone bariatric surgery;
b. non-obese group: subject must have a BMI ≥18.5 and <30 kg/m2 at the time of inclusion;
2. Subject is at least 18 of age on the day of screening and not older than 65 years of age on the day of dosing

Pre-assignment

Screening details:

At screening, medical and surgical history, concomitant diseases, anthropomorphic data (weight, height, sex, month and year of birth), clinical diagnosis and concomitant drugs will be reported

Period 1

Period 1 title	Screening + inclusion phase (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Individuals with obesity

Arm description:

Patients scheduled for bariatric surgery with BMI >35

Arm type	Experimental
Investigational medicinal product name	fluconazole 400mg capsule
Investigational medicinal product code	
Other name	Diflucan
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Oral administration 400mg

Investigational medicinal product name	Fluconazole 400mg infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 400mg administered over 20 minutes, starting 2h after the oral administration

Arm title	non-obese control patients

Arm description:

Normal weight healthy volunteers

Arm type	Active comparator
Investigational medicinal product name	fluconazole 400mg capsule
Investigational medicinal product code	
Other name	Diflucan
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details: Oral administration 400mg	
Investigational medicinal product name	Fluconazole 400mg infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 400mg administered over 20 minutes, starting 2h after the oral administration

Number of subjects in period 1	Individuals with obesity	non-obese control patients
Started	17	8
completed	17	8
Completed	17	8

Baseline characteristics

Reporting groups	
Reporting group title	Individuals with obesity
Reporting group description:	
Patients scheduled for bariatric surgery with BMI >35	
Reporting group title	non-obese control patients
Reporting group description:	
Normal weight healthy volunteers	

Reporting group values	Individuals with obesity	non-obese control patients	Total
Number of subjects	17	8	25
Age categorical			
Age			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	8	25
From 65-84 years	0	0	0
85 years and over	0	0	0
obese	0	0	0
Gender categorical			
Units: Subjects			
Female	9	5	14
Male	8	3	11

End points

End points reporting groups	
Reporting group title	Individuals with obesity
Reporting group description: Patients scheduled for bariatric surgery with BMI >35	
Reporting group title	non-obese control patients
Reporting group description: Normal weight healthy volunteers	

Primary: Influence of body weight on fluconazoel pharmacokinetics	
End point title	Influence of body weight on fluconazoel pharmacokinetics
End point description: A full PK-curve after oral and intravenous administration of fluconazole will be obtained in obese and non-obese individuals. Nonlinear mixed effects modelling will be employed to evaluate differences in PK parameters between obese and non-obese individuals	
End point type	Primary
End point timeframe: n.a.	

End point values	Individuals with obesity	non-obese control patients		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	8		
Units: mg/L				
number (not applicable)				
Clearance	1.21	0.94		
Volume of distribution	58.8	40.6		

Attachments (see zip file)	Figure 1: individual concentration time profiles/FIG 1.PNG

Statistical analyses

Statistical analysis title	NONMEM
Statistical analysis description: nonlinear mixed effects modelling	
Comparison groups	Individuals with obesity v non-obese control patients
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	Chi-squared
Parameter estimate	Log likelihood ratio
Point estimate	0.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.214
upper limit	0.532
Variability estimate	Standard deviation
Dispersion value	30

Notes:

[1] - Nonlinear mixed effects modelling

[2] - n.a.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
<24 hours	
Adverse event reporting additional description:	
Adverse events will be reported to the medical supervisor within 24 hours.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	Extravasation
Reporting group description:	
Extravasation of IMP	

Serious adverse events	Extravasation		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Extravasation		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Product issues			
Extravasation	Additional description: Extravasation of the IMP		
alternative dictionary used: MedDRA 26			
subjects affected / exposed	1 / 1 (100.00%)		
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? No

Limitations and caveats

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

n.a.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35613035