Clinical trial results:
The influence of gastrointestinal lipid digestion on the intraluminal behavior of abiraterone (acetate) in healthy volunteers

Summary

EudraCT number	2019-003460-50
Trial protocol	BE
Global end of trial date	12 August 2021

Results information

Result version number	v1 (current)
This version publication date	20 June 2024
First version publication date	20 June 2024

Trial information

Trial identification

Sponsor protocol code	DDD19ABI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	UZ Leuven Clinical Trial Center: S63186

Notes:

Sponsors

Sponsor organisation name	KU Leuven Drug Delivery and Disposition
Sponsor organisation address	Gasthuisberg ON2 | Herestraat 49 box 921, Leuven, Belgium, 3000
Public contact	Patrick Augustijns, KU Leuven Drug Delivery & Disposition, +32 16330301, patrick.augustijns@kuleuven.be
Scientific contact	Patrick Augustijns, KU Leuven Drug Delivery & Disposition, +32 16330301, patrick.augustijns@kuleuven.be

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	03 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 August 2021
Global end of trial reached?	Yes
Global end of trial date	12 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the influence of lipid digestion on the gastrointestinal and systemic disposition of abiraterone (acetate) following oral intake of Zytiga in healthy, male volunteers.

Protection of trial subjects:

Standard procedures for placement of nasogastric tubes to aspirate gastrointestinal fluids and a venous catheter to sample systemic blood.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2021
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	Belgium: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy volunteers were recruited in March-August 2021 following a public announcement at the university campus (Leuven, Belgium).

Pre-assignment

Screening details:

Candidate participants were screened for in- and exclusion criteria.
Inclusion: male, 18-40 years old, healthy.
Exclusion: female, illness at the time of study, medication use (in particular CYP3A4 inducers), history of acute/chronic gastrointestinal, liver or cardiovascular disease(s), infection with HIV, HBV, HCV

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?	No
Arm title	Fasted state

Arm description:

Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fasted state conditions.

Arm type	Experimental
Investigational medicinal product name	abiraterone acetate (Zytiga)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Abiraterone acetate (500 mg) was administered as 1 tablet of Zytiga with 240 mL of water.

Arm title	Fed state

Arm description:

Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fed state conditions (intake of an Ensure Plus liquid meal).

Arm type	Experimental
Investigational medicinal product name	abiraterone acetate (Zytiga)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Abiraterone acetate (500 mg) was administered as 1 tablet of Zytiga with 240 mL of water, 20 min after intake of the liquid meal Ensure Plus.

Arm title	Fasted state + inhibition lipolysis

Arm description:

Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fasted state conditions and upon administration of the lipase inhibitor orlistat (Xenical, 2x 120 mg)

Arm type	Experimental

Investigational medicinal product name	abiraterone acetate (Zytiga)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Abiraterone acetate 500 mg was administered as 1 tablet of Zytiga with 240 mL of water, 20 min after intake of a capsule of Xenical (orlistat 120 mg). Two hours after intake of Zytiga, a second Xenical capsule was administered.

Arm title	Fed state + inhibition lipolysis

Arm description:

Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fed state conditions and upon administration of the lipase inhibitor orlistat (Xenical, 2x 120 mg)

Arm type	Experimental
Investigational medicinal product name	abiraterone acetate (Zytiga)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Abiraterone acetate 500 mg was administered as 1 tablet of Zytiga with 240 mL of water, 20 min after intake of the liquid meal Ensure Plus and a capsule of Xenical (orlistat 120 mg). Two hours after intake of Zytiga, a second Xenical capsule was administered.

Number of subjects in period 1	Fasted state	Fed state	Fasted state + inhibition lipolysis
Started	4	5	4
Completed	4	5	4

Number of subjects in period 1	Fed state + inhibition lipolysis
Started	4
Completed	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	5	5	

End points

End points reporting groups

Reporting group title	Fasted state
Reporting group description:	
Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fasted state conditions.	
Reporting group title	Fed state
Reporting group description:	
Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fed state conditions (intake of an Ensure Plus liquid meal).	
Reporting group title	Fasted state + inhibition lipolysis
Reporting group description:	
Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fasted state conditions and upon administration of the lipase inhibitor orlistat (Xenical, 2x 120 mg)	
Reporting group title	Fed state + inhibition lipolysis
Reporting group description:	
Disposition of abiraterone following oral intake of 1 tablet of Zytiga (abiraterone acetate 500 mg) in fed state conditions and upon administration of the lipase inhibitor orlistat (Xenical, 2x 120 mg)	

Primary: Systemic AUC abiraterone

End point title	Systemic AUC abiraterone[1]
End point description:	
End point type	Primary
End point timeframe:	
0-24 h post drug intake	

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: The study was designed as exploratory without power to statistically test hypotheses.

End point values	Fasted state	Fed state	Fasted state + inhibition lipolysis	Fed state + inhibition lipolysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4[2]	4	4
Units: nM*h				
arithmetic mean (standard deviation)	803 (± 301)	2490 (± 373)	655 (± 477)	2405 (± 494)

Notes:

[2] - The subject only participating in 1 arm of the study was excluded from the analyses.

Statistical analyses

No statistical analyses for this end point

Primary: Jejunal AUC abiraterone

End point title	Jejunal AUC abiraterone[3]
End point description:	

End point type	Primary

End point timeframe:

0-5 h post drug intake

Notes:

[3] - 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: The study was designed as exploratory without power to statistically test hypotheses.

End point values	Fasted state	Fed state	Fasted state + inhibition lipolysis	Fed state + inhibition lipolysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	4
Units: µM*min				
arithmetic mean (standard deviation)	9011 (± 5468)	16044 (± 3344)	7684 (± 2960)	10609 (± 2240)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: From first visit of first subject till last visit of last subject.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Frequency threshold for reporting non-serious adverse events: 5 %

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: No adverse events happened during this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2021	- Restart of clinical trial after outbreak of the COVID-19 pandemic, including specific measures to minimize the risk on COVID-19 transmission during positioning of the gastrointestinal catheters. - Use of an optimized catheter design, enabling positioning of the catheter at the day of the study (instead of the previous day).

Notes:

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.

Exploratory, small scale study with no power to statistically test hypotheses.

Notes: