



## Clinical trial results:

### Pharmacokinetics, safety and efficacy of atazanavir /dolutegravir/lamivudine regimen as maintenance regimen in pa-tients with intolerance and/or resistance to NRTIs, NNRTIs and RTV: a pilot study (PRADA II study)

#### Summary

EudraCT number	2014-004488-19
Trial protocol	NL
Global end of trial date	27 December 2016

#### Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019
Summary attachment (see zip file)	PRADA abstract P31 (2016_6.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	UMCN-AKF-14.08
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands,
Public contact	David Burger, Radboud University Medical Center, +31 243616405, david.burger@radboudumc.nl
Scientific contact	David Burger, Radboud University Medical Center, +31 243616405, david.burger@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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	27 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 December 2016
Global end of trial reached?	Yes
Global end of trial date	27 December 2016
Was the trial ended prematurely?	Yes

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the pharmacokinetics of the alternative maintenance QD regimen combining atazanavir, dolutegravir and lamivudine in HIV infected patients.

Protection of trial subjects:

The risk-classification is assessed as 'moderate' to the patient population receiving study drug at the current regimen. The drugs are licensed on the Dutch market for the dose administered. Atazanavir 400 mg once daily with food is licensed in de US. The study participants are HIV-1 infected patients who experience side-effects or intolerance to their current regimen. Switching to a new maintenance regimen can potentially reduce toxicities and/or side-effects. The participants will thus benefit from the participation in this clinical trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

Notes:

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**Subjects enrolled per age group**

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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)	9
From 65 to 84 years	0

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

HIV-infected adult, in need for a switch in maintenance regimen due to adverse effects, toxicities, simplification and/or resistance.

### Period 1

Period 1 title	screening
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	PRADA II regime
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Arm description: -

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

Dosage and administration details:

50 mg QD

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

Dosage and administration details:

400 mg QD

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

Dosage and administration details:

300mg QD

<b>Number of subjects in period 1</b>	PRADA II regime
Started	9
Completed	9

<b>Period 2</b>	
Period 2 title	PK day
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
<b>Arms</b>	
<b>Arm title</b>	PK day treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	dolutegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50 mg QD	
Investigational medicinal product name	atazanavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
400 mg QD	
Investigational medicinal product name	lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
300mg QD	

Number of subjects in period 2	PK day treatment
Started	9
Completed	9

**Period 3**

Period 3 title	adult data
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

**Arms**

<b>Arm title</b>	PRADA II regime
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	dolutegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50 mg QD	
Investigational medicinal product name	atazanavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
400 mg QD	
Investigational medicinal product name	lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
300mg QD	

<b>Number of subjects in period 3</b>	PRADA II regime
Started	9
Completed	1
Not completed	8
not applicable, literature data	8

## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	PRADA II regime
Reporting group description: -	
Reporting group title	PK day treatment
Reporting group description: -	
Reporting group title	PRADA II regime
Reporting group description: -	

### Primary: DTG trough levels

End point title	DTG trough levels <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe:	
24h after dosing on PK day	

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: no formal statistical analysis was done, just descriptive

End point values	PK day treatment	PRADA II regime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: mg/L				
geometric mean (geometric coefficient of variation)	2.96 (± 71)	1 (± 77)		

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

entire study

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	none
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Dictionary version	1
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### Reporting groups

Reporting group title	PRADA II
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Reporting group description: -

Serious adverse events	PRADA II		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
pneumocystitis jiroveci pneumonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PRADA II		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
Nervous system disorders			
headache			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 September 2016	Because of availability of an even more simplified treatment regimen: dolutegravir + lamivudine, we stopped this study.	-

Notes:

### Limitations and caveats

None reported