Clinical trial results:
Randomized,multicenter,open-label, study of monoterapy with darunavir/ritonavir or lopinavir/ritonavir vs standard of care in virologically suppressed HIV-infected patients.

Summary

EudraCT number	2012-004556-11
Trial protocol	IT
Global end of trial date	03 August 2015

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020
Summary attachment (see zip file)	2pm new microbiologica (2pm new microbiologica.pdf)

Trial information

Trial identification

Sponsor protocol code	2PM

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ospedal San Raffaele Srl
Sponsor organisation address	Via Stamira d'Ancona 20, Milan, Italy,
Public contact	Malattie Infettive, Ospedale San Raffaele, 0039 0226437906, gianotti.nicola@hsr.it
Scientific contact	Malattie Infettive, Ospedale San Raffaele, 0039 0226437906, gianotti.nicola@hsr.it

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	01 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2015
Global end of trial reached?	Yes
Global end of trial date	03 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to demonstrate the non-inferiority of two different regimes of simplification of HAART monotherapy with PI / r (darunavir / ritonavir and lopinavir / ritonavir) compared to HAART therapy in patients with HIV infection treated with any regimen PI based and viral replication completely suppressed.

Protection of trial subjects:

Study approved by local Ethics Committee as per current regulatory laws. Patient signed Informed consent ; no invasive procedures performed. Data of patients were anonymised.

Background therapy:

no in the experimental arm. Control arm was standard of care

Evidence for comparator:

Comparator= standard of care according to national and international guidelines

Actual start date of recruitment	01 March 2012
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	Italy: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	43
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Forty-five patients were screened between June 2013 and July 2014; two patients did not meet eligibility criteria and were not randomized; 43 were randomized.

Pre-assignment

Screening details:

HIV-infected adults receiving cART, virologically suppressed, current CD4+ >200 cells/μL and nadir CD4+ >100 cells/μL were included in the study.
Main exclusion criteria were the detection at any time of any DRV-resistance, previous virological failure, HBsAg+, ongoing cancer, pregnancy, breestfeeding.

Period 1

Period 1 title	June 2013-July 2014 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DRV monotherapy

Arm description:

Monotherapy of Darunavir/ritonavir 800 mg/100 mg once daily (DRV/r-MT arm)

Arm type	Experimental
Investigational medicinal product name	Monotherapy of Darunavir/ritonavir 800 mg/100 mg once daily (DRV/r-MT arm)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Monotherapy of DRV/r 800 mg/100 mg once daily (DRV/r-MT arm)
Monotherapy with LPV/r 400mg/100mg twice daily (LPV/r-MT arm)

Arm title	LPV/r monotherapy

Arm description:

Monotherapy with Lopinavir/ritonavir 400mg/100mg twice daily (LPV/r-MT arm)

Arm type	Experimental
Investigational medicinal product name	Monotherapy with Lopinavir/ritonavir 400mg/100mg twice daily (LPV/r-MT arm)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Monotherapy with Lopinavir/ritonavir 400mg/100mg twice daily (LPV/r-MT arm)

Arm title	Control Arm

Arm description:

Control Arm as per standard of care

Arm type	Active comparator

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

Dosage and administration details:

Standard of care therapy as per national and international guidelines

Number of subjects in period 1	DRV monotherapy	LPV/r monotherapy	Control Arm
Started	15	13	15
Completed	13	10	13
Not completed	2	3	2
Consent withdrawn by subject	1	3	1
Adverse event, non-fatal	-	-	1
Pregnancy	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	DRV monotherapy
Reporting group description:	
Monotherapy of Darunavir/ritonavir 800 mg/100 mg once daily (DRV/r-MT arm)	

Reporting group title	LPV/r monotherapy
Reporting group description:	
Monotherapy with Lopinavir/ritonavir 400mg/100mg twice daily (LPV/r-MT arm)	
Reporting group title	Control Arm
Reporting group description:	
Control Arm as per standard of care	

Reporting group values	DRV monotherapy	LPV/r monotherapy	Control Arm
Number of subjects	15	13	15
Age categorical 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)	15	13	15
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	6	2	2
Male	9	11	13

Reporting group values	Total		
Number of subjects	43		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	43		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	10		
Male	33		

End points

End points reporting groups

Reporting group title	DRV monotherapy
Reporting group description:	
Monotherapy of Darunavir/ritonavir 800 mg/100 mg once daily (DRV/r-MT arm)	

Reporting group title	LPV/r monotherapy
Reporting group description:	
Monotherapy with Lopinavir/ritonavir 400mg/100mg twice daily (LPV/r-MT arm)	

Reporting group title	Control Arm
Reporting group description:	
Control Arm as per standard of care	

Primary: Primary endpoint

End point title	Primary endpoint[1]
End point description:	
proportion with virological success according to the Snapshot FDA algorithm	
End point type	Primary
End point timeframe:	
48 weeks	

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: proportion with virological success according to the Snapshot FDA algorithm

End point values	DRV monotherapy	LPV/r monotherapy	Control Arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	15	
Units: proportion				
virological success	73	69	87	
virological failure	0	8	0	
No data in window	27	23	13	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 48 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	Free language
Dictionary version	1
Reporting groups	
Reporting group title	DRV monotherapy
Reporting group description: Monotherapy of Darunavir/ritonavir 800 mg/100 mg once daily (DRV/r-MT arm)	
Reporting group title	LPV/r monotherapy
Reporting group description: Monotherapy with Lopinavir/ritonavir 400mg/100mg twice daily (LPV/r-MT arm)	
Reporting group title	Control Arm
Reporting group description: Control Arm as per standard of care	

Serious adverse events	DRV monotherapy	LPV/r monotherapy	Control Arm
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	DRV monotherapy	LPV/r monotherapy	Control Arm
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	2 / 13 (15.38%)	4 / 15 (26.67%)
Endocrine disorders			
dyslipidemia			
alternative assessment type: Non-systematic			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	2 / 13 (15.38%) 2	1 / 15 (6.67%) 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? Yes

Date	Interruption	Restart date
31 July 2014	Due to the slow recruitment rate, enrolment was interrupted after two years. For this reason the non-inferiority of the two MT regimens versus standard antiretroviral therapy could not be assessed.	-

Notes:

Limitations and caveats

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

Due to the slow recruitment rate, enrolment was interrupted after two years. For this reason the non-inferiority of the two MT regimens versus standard antiretroviral therapy could not be assessed.

Notes: