Clinical trial results: *Full title of Trial**

Summary

EudraCT number*	2008-006287-11
Trial protocol	VEMAN Study "Maraviroc 150 mg daily plus lopinavir/ritonavir regimen for HIV infected naïve patients"
Global end of trial date*	30/01/2015

Trial information

Trial identification	
Sponsor protocol code*	VEMAN Study (HSR)
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	na
WHO universal trial number (UTN)	-

Notes:

Sponsors details*	
Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	nozza.silvia@hsr.it
Scientific contact	Nozza Silvia – Lazzarin Adriano

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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Results analysis stage	
Analysis stage*	Final
Date of interim/final analysis*	Weeks 48
Is this the analysis of the primary completion data?*	Yes or No
Global end of trial reached?*	Yes or No
Global end of trial date*	
Was the trial ended prematurely?	Yes or No

General information about the trial

Main objective of the trial*: *Enter a description for the mail objective(s) of the trial*

Actual start date of recruitment*	20/02/2009 Authorized on 08/05/2009
Long term follow-up planned*	No
If Yes, rationale:	Safety Efficacy Ethical reason Regulatory reason Scientific research
Duration	48 weeks follow-up final results
Independent data monitoring committee (IDMC) involvement?*	No
Protection of trial subjects*:	VEMAN is a proof of principle study, with a small sample size; as a result, although the study was not powered to highlight statistical differences, the virological efficacy and safety seemed to be similar in the two study groups and these results are better than other small studies with NRTI-sparing regimens containing maraviroc.
Background therapy:	

Population of trial subjects

Subjects enrolled per country

Country:	Italy
Planned number of subjects	15
Actual Number of subjects enrolled*	38 OSR (50 patients in total distributed in to 4 Italian sites)
Worldwide total number of subjects	
EEA total number of subjects	

Subjects enrolled per age group

In utero*	0
Preterm newborn - gestational age < 37wks*	0
Newborns (0-27 days)*	0
Infants and toddlers (28 days-23months)*	0
Children (2-11 years)*	0
Adolescents (12-17 years)*	0
Adults (18-64 years)*	38 IRCCS Ospedale San Raffaele
From 65 to 84 years*	0
85 years and over*	0

Subject disposition

Recruitment details: *Enter key information relevant to the recruitment process for the trial (eg gates of recruitment period and territories)*

This was a proof-of-principle, multicentre, randomized, openlabel,active-controlled, parallel-group study conducted in four Italian sites.
All eligible patients were randomized 1:1 using a computerized random-number-generator program to receive maraviroc 150 mg once daily plus lopinavir/ritonavir 400/100 mg twice daily (MVC group) or tenofovir/emtricitabine plus lopinavir/ ritonavir 400/100 mg twice daily (TDF/FTC group).

STUDY POPULATION; Adult, treatment-naive, HIV-1 infected patients, CD4 count _100 cells/μL, HIV-RNA _1000 copies/mL were screened using the Trofile assay (Monogram Biosciences, San Francisco,CA, USA); only patients with CCR5 tropic virus were enrolled and randomized to the study treatments.

Pre-assignment - *Screening details*: *Enter relevant information related to screening (eg screening criteria, significant events and approaches)*

Period 1	
Period title*	*Enter a title describing the stage of the trial. If the only one period is defined, the default title should be "Overall Trial"*
Is this the baseline period?	Yes or No
Allocation method*	Randomized openlabel,active-controlled, parallel-group
Blinding used*	Not blinded

Arms

Arm title*	***Maraviroc plus Lopinavir/ritonavir***
Arm description:	*MVC Group*
Arm type*	Intervention treatment arm
Investigational medicinal product name*	**Celsentri + Kaletra**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**CPR**
Routes of administration*	**oral**
Dosage and administration details*	MVC 150 mg QD + LPV/R

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	50	26 patients in MVC Group + 24 patients in TDF/FTC plus LPV/R Group
Completed*	45	24 patients in MVC Group + 21 patients in TDF/FTC plus LPV/R Group
Subject non-completion reason (if applicable)		
AE, non fatal		
AE, fatal		
Consent withdrawn by subject		
Lack of efficacy		
Lost to follow up		
Physician decision		

Pregnancy		
Protocol Deviation		
Other		

Baseline characteristics

Reporting groups* Overall cohort	
Reporting group title*	
Number of subjects at the baseline*	**See TABLE 1 CMI**

Reporting group description: *You can report per arm in the baseline period or for the overall baseline period*

TABLE I. Baseline characteristics of the patients.

Baseline characteristics	Overall (n = 50)	MVC plus LPV/r (n = 26)	TDF/FTC plus LPV/r (n = 24)	p value
Gender n (%)				
Male	48 (96%)	25 (96.2%)	23 (95.8%)	0.999
Female	2 (4%)	1 (3.8%)	1 (4.2%)	
Age at last visit (years)	39.1 (32.4–44)	38.9 (34.2–44)	39.4 (34.3–43.5)	0.961
Risk factors, n (%)				
MSM	38 (76%)	19 (73.1%)	19 (79.2%)	0.745
Heterosexual	12 (24%)	7 (26.9%)	5 (20.8%)	
HIV infection (years)	2.9 (0.8–5.3)	2.9 (0.6–7.2)	2.9 (0.9–4.6)	0.459
Nadir $CD4^+$ (cells/mL)	266 (242–315)	269 (249–321)	263 (230–308)	0.547
CD4 (cells/mL)	295 (260–369)	292 (261–359)	297 (257–373)	0.676
CD4 %	18.8 (14.6–23)	19.5 (16.3–24.3)	18.8 (14.3–22.3)	0.756
CD4/CD8	0.33 (0.25–0.47)	0.35 (0.25–0.48)	0.33 (0.28–0.4)	0.793
HIV-RNA (log_{10} copies/ml)	4.41 (3.96–4.8)	4.42 (4.07–4.84)	4.41 (3.84–4.76)	0.420
AST (U/L)	23 (20–29)	26 (21–37)	23 (19–26)	0.033
ALT (U/L)	27 (21–38)	34 (21–61)	25 (20–30)	0.045
CPK (U/L)	98 (73–147)	114 (73–165)	114 (73–165)	0.214
Creatinine (mg/dL)	0.83 (0.77–0.95)	0.83 (0.78–0.98)	0.83 (0.77–0.95)	0.641
Cholesterol (mg/dL)	171 (145–200)	178 (149–204)	160 (144–194)	0.236
LDL cholesterol (mg/dL)	100 (82–129)	105 (86–140)	100 (82–128)	0.386
HDL cholesterol (mg/dL)	40 (35–50)	38 (36–53)	41 (35–47)	0.622
Triglycerides (mg/dL)	91 (64–143)	91 (64–126)	91 (66–128)	0.831
Glucose (mg/dL)	83 (77–91)	81 (75–89)	84 (78–91)	0.268

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MSM men who have sex with men; MVC plus LPV/r, maraviroc plus lopinavir/ritonavir; TDF/FTC plus LPV/r, tenofovir/emtricitabine plus lopinavir/ritonavir.

Subject analysis sets

Add a subject analysis set if you wish to report on groups different from the reporting group defined above (repeat if applicable)

Subject analysis set title*	
Subject analysis set type*	Full Analysis **Intention to treat** Per protocol Safety analysis Sub-group analysis
Subject analysis set description*	The sample size for this pilot trial was based primarily on feasibility considerations. This pilot randomized controlled trial will inform the estimates of effect sizes and variance for a larger trial. Results were described as median (interquartile range) or frequency (%), as appropriate. The primary analysis considered the primary endpoint and was performed according to the intention-to-treat principle, including all randomized subjects. Changes were calculated within each treatment group and significant variations were assessed by the Wilcoxon signed rank test.
Number of subjects in subjects analysis set*	*50*

Age characteristics*

Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.

	Characteristic title*	Units*	Age categories*
Age categorical	48	age	years

	Characteristic title*	Units*	Central tendency*	Dispersion type*
Age continuous	Overall cohort	Years Months Weeks Days	Arithmetic Mean Median least square mean geometric mean log mean	full range (min-max) standard deviation inter quartile range

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	M F	M F	Male Female

Study specific characteristics

	Characteristic title*	Units *	Categories*	Number of subject for each categories
Study specific categorical				
Study specific categorical				
Study specific categorical				
Study specific categorical				
Study specific categorical				

End points

Add subject analysis set if you wish to report on groups different form reporting groups defined above

Subject analysis set title*	
Subject analysis set type*	Full Analysis **Intention to treat** Per protocol Safety analysis Sub-group analysis
Subject analysis set description*	The primary endpoint was the 12-week change of HIV-1 RNA from baseline. Secondary endpoints, evaluated at weeks 12, 24, 36 and 48, were: the proportion of participants with HIV-1 RNA <50 copies/mL; change from baseline in HIV-1 RNA; change from baseline of immunological parameters; and change from baseline in all the considered safety parameters
Number of subject in subject analysis set *	50

End points definitions

End point title*	the 12-week change of HIV-1 RNA from baseline.	
		Values
Countable or measurable?*	*Measurable*	-
If countable, Countable units*:		
If measurable, Measurable units*		
Measure type*:	Number Arithmetic Mean **Median** least square mean geometric mean log mean	
Precision/dyspersion type*		

End point type*	**Primary** Secondary Other pre-specified Post Hoc

End point timeframe*: 12 weeks

End point title*	the proportion of participants with HIV-1 RNA <50 copies/mL; change from baseline in HIV-1 RNA; change from baseline of immunological parameters;	
		Values
Countable or measurable?*		-
If countable, Countable units*:		
If measurable, Measurable units*		
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	
Precision/dyspersion type*		

End point type*	Primary **Secondary** Other pre-specified Post Hoc

End point timeframe*: 12, 24, 36 and 48 weeks

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*			
Period			
Arms			
subject analysis sets			

Adverse events

Adverse events information

Timeframe for reporting adverse events*: *Enter the time point(s) or time period for AE assessment*

First patient first visit: UNK 2009
Last recruitment date: Follow up extended into 96 weeks only for IRCCS Ospedale San Raffaele (2011)
Study closure: 30/01/2015

Adverse event reporting additional description: *Enter information about the AE collection and provide details about the method of assessment and monitoring*

Five patients stopped treatment (two in the MVC group and three in the TDF/FTC group) at week 24 for diarrhoea when viral load was undetectable (HIV RNA<50 copies/mL). Treatment was well tolerated and trends of bone marrow function, aspartate aminotransferase, alanine aminotransferase and creatine phosphokinase values, creatinine, glucose profile and lipid profile during follow up were not clinically significantly different between the two groups.

Assessment type*	
Frequency threshold for reporting non-serious adverse events*	*Enter the frequency of non SAE that are reported in the results database for all arms or reporting groups*

Dictionary used

Dictionary name*	MedDRA or CTCAE
Dictionary version*	

Adverse events reporting group definition

Use arms from baseline period as reporting groups
OR

Reporting group title*: *Overall cohort*

For this reporting group, provide the following totals:

Subject exposed*	
Subjects affected by non -SAE*	
Total number of deaths (all causes)*	
Total number of deaths resulting from adverse event*	

Serious adverse event details and values

System organ class*:

Event term*:

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number

Non - Serious adverse event details and values

System organ class*:

Event term*:

Values for non-serious adverse event per reporting group*

Threshold for non-serious adverse event reporting is:

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? Yes or No

Date	Amendment
04/03/2010	01
07/04/2011	Addendum ICF San Raffaele Hospital

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? Y e s o r No

If Yes, Interruption date

Interruption descrption

Limitations and caveats

None reported

Online references

Nozza S, Galli L, Antinori A, Chiappetta S, Mazzotta F, Zaccarelli M, Ottou S, De Battista D, Pogliaghi M, Di Pietro M, Malnati M, Ripa M, Bonora S, Lazzarin A; VEMAN Study Group. Maraviroc 150 mg daily plus lopinavir/ritonavir, a nucleoside/nucleotide reverse transcriptase inhibitor-sparing regimen for HIV-infected naive patients: 48-week final results of VEMAN study. Clin Microbiol Infect. 2015 May;21(5):510.e1-9. doi: 10.1016/j.cmi.2014.12.006. Epub 2014 Dec 11. PMID: 25656621.