Clinical trial results: *Full title of Trial**

Summary

EudraCT number*	2008-007004-29
Trial protocol	Maraviroc in HIV Acute INfection
Global end of trial date*	22 mar 2012

Trial information

Trial identification	
Sponsor protocol code*	Maraviroc in HIV Acute Infection (MAIN 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 – Tambussi Giuseppe

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 and 96
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*	12/11/2009 Authorized on 20 Feb 2009
Long term follow-up planned*	No
If Yes, rationale:	Safety Efficacy Ethical reason Regulatory reason Scientific research
Duration	96 weeks follow-up
Independent data monitoring committee (IDMC) involvement?*	No
Protection of trial subjects*:	The MAIN (Maraviroc in HIV Acute INfection) study was a randomized open-label clinical trial (EUDRACT number: 2008-007004-29) which enrolled 29 patients with PHI. Subjects were randomly assigned to receive cART-only (cART), cART + 8 weeks of MVC (ST-MVC) or cART + 48 weeks of MVC (LTMVC), regardless of predicted co-receptor usage. After 48 weeks patients in ST-MVC and LT-MVC groups discontinued MVC. Patients were evaluated at week 48 and at week 96 of follow-up to assess differences in CD4 T-cell gain and plasma HIV-RNA.

Population of trial subjects

Subjects enrolled per country

Country:	Italy
Planned number of subjects	45
Actual Number of subjects enrolled*	29
Worldwide total number of subjects	29
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)*	29
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)*

Symptomatic or asympotamic patient with positive p24 antigenemia, HIV infection, initiating of therapy within 72 hours of diagnosis of PHI

Twenty-nine patients were enrolled. Seven patients (24%) had a predicted CXCR4 co-receptor usage. At week 48, 27 patients (93.1%) reached HIV-RNA <50cps/mL. Median CD4 T-cell count increase was 313 cells/_L ($p < 0.001$, Wilcoxon signed-rank test). At multivariate linear regression analysis, LTMVC arm had the greatest CD4 T-cell increase, while patients in ST-MVC arm had the least gain in CD4 T-cells ($p = 0.007$). At week 96, multivariate analysis showed no associations between former treatment arm and CD4 T-cell gain.

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*	Randomised – open label
Blinding used*	Not blinded

Arms	
Arm title*	*MARAVIROC*
Arm description:	
Arm type*	Intervention treatment arm
Investigational medicinal product name*	**Celsentri**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**CPR**
Routes of administration*	**oral**
Dosage and administration details*	Standard doses

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	29	
Completed*	29	
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**

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

Table 1
Baseline characteristics.

Characteristics	cART (N = 10)	ST-MVC (N = 9)	LT-MVC (N = 10)	OVERALL (N = 29)	P
Age	33 (26/36)	44 (37/49)	41 (37/49)	39 (34/46)	**0.003**[a]
Sex					0.617[b]
M	9 (90%)	9 (100%)	9 (90%)	27 (93%)	
F	1 (10%)	0 (0%)	1 (10%)	2 (7%)	
Risk factor					0.215[b]
MSM	6 (60%)	2 (22%)	4 (40%)	12 (41%)	
Heterosexuals	1 (10%)	5 (56%)	5 (50%)	11 (38%)	
Other	3 (30%)	2 (22%)	1 (10%)	6 (21%)	
Fiebig					0.063[b]
III	2 (20%)	7 (78%)	2 (20%)	11 (38%)	
IV	1 (10%)	0 (0%)	1 (10%)	2 (7%)	
V	7 (70%)	2 (22%)	7 (70%)	16 (55%)	
Predicted co-receptor usage					0.201[b]
CCR5	9 (90%)	5 (56%)	8 (80%)	22 (76%)	
CXCR4	1 (10%)	4 (44%)	2 (20%)	7 (24%)	
CD4, cells/μL	493 (268/698)	330 (243/412)	425 (303/602)	398 (268/586)	0.276[a]
CD4%	15.8 (10.1/28.4)	27.2 (12.9/36.7)	15.8 (9.9/26.7)	18.4 (11.0/28.6)	0.254[a]
CD8, cells/μL	1405 (738/2617)	578 (229/1380)	1872 (794/3117)	1162 (594/2398)	0.054[a]
CD8%	57.1 (45.5/71.9)	42.6 (29.2/65.8)	70.8 (49.1/72.7)	55.8 (39.4/72.2)	0.199[a]
CD4:CD8	0.33 (0.16/0.65)	0.70 (0.20/0.97)	0.22 (0.13/0.55)	0.33 (0.16/0.73)	0.186[a]
HIV-RNA, log10 cp/mL	5.58 (5.11/6.51)	6.36 (5.86/6.92)	5.73 (4.90/7.01)	6.07 (5.14/6.77)	0.324[a]

[a] By Kruskal-Wallis test.
[b] By Chi-Square test.

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 (proof of concept)** Safety analysis Sub-group analysis
Subject analysis set description*	*Enter a clear description which defines this set of subjects*
Number of subjects in subjects analysis set*	*29*

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	34/46	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	Female Male

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*	
Number of subject in subject analysis set *	

End points definitions

End point title*		
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	-
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*:

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: 12/11/2009
Last recruitment date: 22/03/2012
Study closure: 20/03/2024

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

No significant toxicity was recorded in terms of kidney and liver function tests: creatinine levels slightly increased [0.10 mg/dL (0.02/0.13), p = 0.001], never reaching eGFR <90 mL/min/1.73m.

Assessment type*	Systematic or Non Systematic
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*:

Two serious adverse events were recorded: acute hepatitis A occurred in cART arm and VII cranial nerve paralysis in ST-MVC arm, possibly related to MVC; both events required treatment discontinuation.

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
cART-only (N=10)	1	10	1	0	0	0
ST-MVC (N=9)	1	9	1	1 (possibly related to MVC)	0	0
LT-MVC (N=10)	0	10	0	0	0	0
Total (N=29)	2	29	2	1	0	0

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
10-11-2010	2.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? Yes or No

If Yes, Interruption date

Interruption descrption

Limitations and caveats

None reported

Online references

Ripa M, Pogliaghi M, Chiappetta S, Nozza S, Soria A, Coppalini G, Rovelli C, Tambussi G. Maraviroc in addition to cART during primary HIV infection: Results from MAIN randomized clinical trial and 96-weeks follow-up. J Clin Virol. 2016 Dec;85:86-89. doi: 10.1016/j.jcv.2016.10.016. Epub 2016 Oct 31. PMID: 27865174.