Clinical trial results:
Optimized Phase III Trial of Immuno-stimulation with Maraviroc, a CCR5 antagonist, combined with Anti Retroviral Therapy (cART) in advanced, Late diagnosed HIV-1 infected patients with an AIDS-defining event and/or CD4 counts below 200 cells/mm3.

Summary

EudraCT number	2010-022293-14
Trial protocol	ES IT
Global end of trial date	31 March 2016

Results information

Result version number	v1 (current)
This version publication date	14 February 2025
First version publication date	14 February 2025
Summary attachment (see zip file)	Summary of final report (RRF engl ANRS 146 OPTIMAL signé.pdf)

Trial information

Trial identification

Sponsor protocol code	ANRS 146 OPTIMAL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01348308
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Inserm-ANRS
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75013
Public contact	Pr. Yves Levy, Service d'Immunology clinique GHU Chenevier-Mondor, +33 1 49 81 44 42, yves.levy@hmn.aphp.fr
Scientific contact	Pr. Yves Levy, Service d'Immunology clinique GHU Chenevier-Mondor, +33 1 49 81 44 42, yves.levy@hmn.aphp.fr

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	23 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the clinical benefit of the adjunction of Maraviroc to a combination of antiretroviral therapy in naïve and late diagnosed HIV-1 infected patients.
The clinical benefit is the reduction of the occurrence of a composite outcome consisting of new AIDS-defining event (ADE), Non B or C events, serious non-AIDS events, IRIS and death.

Protection of trial subjects:

This study was conducted in accordance with the updated Declaration of Helsinki, in compliance with the approved protocol and its amendments, the International Council for Harmonisation guideline for Good Clinical Practice (ICH GCP), and French regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 156
Country: Number of subjects enrolled	France: 213
Country: Number of subjects enrolled	Italy: 40
Worldwide total number of subjects	409
EEA total number of subjects	409

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)	392

From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From October 2011 to November 2014, 459 participants were screened and 416 were randomised in this trial.

Pre-assignment

Screening details:

Main criteria:
Inclusion: confirmed HIV-1 infection, at least 18 years, patient naïve from any antiretroviral.
Non-inclusion: current pregnancy, lack of contraceptive method, breast-feeding, current active tuberculosis.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Maraviroc

Arm description:

cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines with Maraviroc.

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

Dosage and administration details:

3 posologies:
1) 150 mg orally twice a day for patients receiving a PI ritonavir-boosted regimen (except Fosamprenavir)
OR
2) 300 mg orally twice a day for patients receiving a Fosamprenavir ritonavir-boosted regimen
OR
3) 600 mg orally twice a day for patients receiving EFV-based regimen

Arm title	Placebo

Arm description:

cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines, with Placebo twice a day. The number of pills will be adapted accordingly to the combined cART regimen.

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

Dosage and administration details:

3 posologies:
1) 150 mg orally twice a day for patients receiving a PI ritonavir-boosted regimen (except Fosamprenavir)

OR
2) 300 mg orally twice a day for patients receiving a Fosamprenavir ritonavir-boosted regimen
OR
3) 600 mg orally twice a day for patients receiving EFV-based regimen

Number of subjects in period 1	Maraviroc	Placebo
Started	202	207
Completed	169	180
Not completed	33	27
Consent withdrawn by subject	1	-
Adverse event, non-fatal	6	9
Death	-	4
Other reasons	21	9
Lost to follow-up	5	4
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Maraviroc
Reporting group description:	
cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines with Maraviroc.	
Reporting group title	Placebo
Reporting group description:	
cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines, with Placebo twice a day. The number of pills will be adapted accordingly to the combined cART regimen.	

Reporting group values	Maraviroc	Placebo	Total
Number of subjects	202	207	409
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)	197	195	392
From 65-84 years	5	12	17
85 years and over	0	0	0
Age continuous			
Units: years			
median	42	42	
full range (min-max)	21 to 70	21 to 74	-
Gender categorical			
Units: Subjects			
Female	28	34	62
Male	174	173	347

End points

End points reporting groups

Reporting group title	Maraviroc
Reporting group description:	
cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines with Maraviroc.	
Reporting group title	Placebo
Reporting group description:	
cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines, with Placebo twice a day. The number of pills will be adapted accordingly to the combined cART regimen.	

Primary: Occurrence of a composite outcome

End point title	Occurrence of a composite outcome
End point description:	
The primary composite end point was the first occurrence of severe morbidity (new ADE, selected serious infections, serious non-ADE [cardiovascular disease, chronic end-stage renal failure, liver failure, non-AIDS-defining cancer except basal and squamous cell skin cancers]), immune reconstitution inflammatory syndrome (IRIS), or death due to any cause. All events were reviewed by an end point review committee whose members were unaware of study group assignments.	
End point type	Primary
End point timeframe:	
During 72 weeks of follow-up.	

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	207		
Units: Number of participants	26	27		

Statistical analyses

Statistical analysis title	Incidence of the first event
Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.67

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Participants reported adverse events during the entire trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Maraviroc

Reporting group description:

cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines with Maraviroc.

Reporting group title	Placebo

Reporting group description:

cART optimised regimen according to the recommended regimen as first line of treatment in most commonly used guidelines, with Placebo twice a day. The number of pills will be adapted accordingly to the combined cART regimen.

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: Non serious adverse events were not coded for this trial.
79/202 participants experienced AE in the Maraviroc arm and 72/207 in the placebo arm.

Serious adverse events	Maraviroc	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 202 (25.25%)	52 / 207 (25.12%)	
number of deaths (all causes)	0	6	
number of deaths resulting from adverse events	0	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Castleman's disease			
subjects affected / exposed	2 / 202 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Kaposi's sarcoma			
subjects affected / exposed	1 / 202 (0.50%)	3 / 207 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant peritoneal neoplasm			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	2 / 202 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboangiitis obliterans			

subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Arterial bypass operation			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteosynthesis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 202 (1.49%)	4 / 207 (1.93%)	
occurrences causally related to treatment / all	1 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	2 / 202 (0.99%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune reconstitution inflammatory syndrome			
subjects affected / exposed	5 / 202 (2.48%)	7 / 207 (3.38%)	
occurrences causally related to treatment / all	5 / 5	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune reconstitution inflammatory syndrome associated tuberculosis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Social problem			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			

subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			

subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomania			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device occlusion			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Fibula fracture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament injury			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Encephalitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianopia homonymous			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Locked-in syndrome			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 202 (0.99%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	2 / 202 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 202 (0.50%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal injury			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer haemorrhage			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhoids			
subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malabsorption			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			

subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	3 / 202 (1.49%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised			
subjects affected / exposed	2 / 202 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	1 / 202 (0.50%)	3 / 207 (1.45%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 202 (0.00%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			

subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral toxoplasmosis			
subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			

subjects affected / exposed	2 / 202 (0.99%)	3 / 207 (1.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Encephalitis viral			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Escherichia sepsis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes dermatitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 202 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histoplasmosis disseminated			

subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infectious colitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leishmaniasis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis cryptococcal			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterial infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			

subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral fungal infection			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 202 (0.50%)	5 / 207 (2.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 202 (1.49%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 202 (0.50%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive multifocal leukoencephalopathy			

subjects affected / exposed	2 / 202 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 202 (0.50%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary syphilis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 202 (0.00%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sinusitis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strongyloidiasis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subcutaneous abscess			
subjects affected / exposed	0 / 202 (0.00%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syphilis			

subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 202 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Maraviroc	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 202 (0.00%)	0 / 207 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2011	The substantial modifications included in the amendment 1 of the protocol are: - correction of an inclusion criterion, to add other tests to confirm HIV-1 infection; - clarification of several non-inclusion criteria; - correction of the delay between the W-4 screening visit and the W0 visit, in the case of patients who need to be rapidly started on treatment; - update of the list of investigators with a change of principal investigator in 3 centres (n° ANRS 018, 052, 090) and a change of head of department for 1 centre (n° ANRS 090); - modification of the information letter, the consent form and the protocol; - update of the lists of scientific board members and key trial correspondents.
15 May 2012	The substantial modifications included in the amendment 2 of the protocol are: - change of sponsor (sponsor becomes Inserm-ANRS); - modification of a non-inclusion criterion; - modification of the dosage of the trial treatment in case of Raltegravir use; - change of the principal investigator of the Bicêtre centre (Pr. Cécile Goujard replaces Dr. Jade Ghosn).
28 September 2012	The substantial modification included in the amendment 3 of the protocol is the increase in the number of patient in France (125 patients instead of 100-110) without increasing the total number of patients to be included in the trial (decrease in the number of patients in Italy from 100 patients to 75).
12 July 2013	The substantial modifications included in the amendment 4 of the protocol are: - increase in the number of patients in France (without increasing the total number of patients to be included in the trial); - extension of the inclusion period in France; - modification of the seminal compartment sub-study; - opening of centre 32 (Hôpital Necker)
14 January 2014	The substantial modification included in the amendment 5 of the protocol is the extension of the inclusion period in France.
11 July 2014	The substantial modifications included in the amendment 6 of the protocol are: - change of the principal investigator in centre 073 and 090; - change in treatment dosage for participants on nevirapine; - update of the Investigator's Brochure; change in trial contact details.
05 November 2014	The substantial modification included in the amendment 7 of the protocol are: - addition of maraviroc dosing for patients on elvitegravir; - addition of two non-voting members to the trial's scientific advisory board; - addition of known side effects of maraviroc in the patient information leaflet.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30102658