Clinical trial results:
NEW ERA STUDY
HIV and Eradication:
A multicenter, open-label, non-randomized trial to evaluate treatment with multi-drug class (MDC) HAART and its impact on the decay rate of latently infected CD4+ T cells

Summary

EudraCT number	2008-002070-35
Trial protocol	DE
Global end of trial date	03 April 2018

Results information

Result version number	v1 (current)
This version publication date	02 November 2019
First version publication date	02 November 2019
Summary attachment (see zip file)	_ (New Era Study_ Treatment With Multi Drug Class (MDC) HAART in HIV Infected Patients - Full Text View - ClinicalTrials.gov.pdf)

Trial information

Trial identification

Sponsor protocol code	MUC_NewEra_3.3

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00908544
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MUC Research GmbH
Sponsor organisation address	Karlsplatz 8, Munich, Germany, 80335
Public contact	MUC Research, MUC Research GmbH, 0049 089558703630, info@mucresearch.de
Scientific contact	MUC Research, MUC Research GmbH, 0049 089558703630, info@mucresearch.de

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	03 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2018
Global end of trial reached?	Yes
Global end of trial date	03 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this trial were to halt residual viral replication in plasma and to deplete HIV DNA in peripheral blood mononuclear cells (PBMC), thereby achieving HIV eradication using MDC (multi-drug class) HAART (Highly Active Antiretroviral Therapy) in patients with primary HIV-infection (PHI patients) and in successfully treated chronically HIV-infected patients (CHI patients) after an overall treatment period of at least 5 years including MDC HAART for at least 2 years.
Further objectives of this trial were to provide good estimates of the latently infected reservoir size (infectious copies/10exp6 PBMC and infectious copies/10exp6 resting CD4+ T cells) and to evaluate the decay rates (i.e. changes) of latently infected PBMC (CD4+ T cells).

Protection of trial subjects:

Patients were asked about all adverse experiences (AEs) at each study visit.
Guidelines for grading the severity of adverse experiences were based on the criteria published by the Division of Acquired Immunodeficiency Syndrome (DAIDS; Version 1.0, December 2004; clarification August 2009).

Background therapy:

Patients with primary HIV infection (PHI) are immediately treated with 2 NRTI + 1 PI/r + study drugs Maraviroc + Raltegravir.
Therapy in patients with chronic HIV infection (CHI) and with suppressed plasma viral load for at least three years under continuous HAART (2 NRTI + 1 PI/r) is intensified by study drugs Maraviroc + Raltegravir.

Evidence for comparator:

Two cooperating HIV-specialized centres represented by Dr. med. Hans Jaeger and Prof. Dr. Johannes Bogner planed to perform an IIT (investigator initiated trial) with the goal to eradicate HIV in N=40 HIV-infected patients with either primary infection or chronic infection and successful HAART (Highly Active Antiretroviral Treatment) of several years. All patients has been started on a multi-drug HAART including two Nucleoside-Reverse-Transcriptase-Inhibitors (NRTI´s), one Protease-Inhibitor (PI), a CCR5-inhibitor and an Integrase-Inhibitor (INI). Decay of viral reservoirs like latently HIV-infected CD4+ T-cells were monitored over time.

Actual start date of recruitment	15 May 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	7 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 47
Worldwide total number of subjects	47
EEA total number of subjects	47

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)	47
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants from 7 clinical sites in Germany were recruited between May 2009 and February 2011.

Pre-assignment

Screening details:

Planned count of participant: 40 patients (20 patients per arm); 58 pts were assessed for eligibility, 11 pts were excluded;
47 were started on study drugs ; 5 pts with primary infection immediately started on study drugs (as defined by the study protocol) turned out to be screening failures;
42 eligible pts continued treatment: 22 PHI, 20 CHI

Pre-assignment period milestones

Number of subjects started	47
Number of subjects completed	42

Pre-assignment subject non-completion reasons

Reason: Number of subjects	non fulfillment of eligiblity criteria: 5

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CHI-group

Arm description:

Patients with chronic HIV infection (CHI) and with suppressed plasma viral load for at least three years under continuous HAART (Highly active antiretroviral treatment) consisting of 2 NRTI + 1 PI/r (see also "Eligibility") intensified by Maraviroc + Raltegravir
CHI-patients: Treatment intensification of PI-based HAART with Maraviroc and Raltegravir.
Therapy: 2 NRTI + 1 PI/r + Maraviroc + Raltegravir

Arm type	Experimental
Investigational medicinal product name	Maraviroc
Investigational medicinal product code	J05AX09
Other name	Celsentri
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosing of antiretrovirals including study drug Maraviroc was according to standard dosing as outlined in respective product informations:
- Maraviroc 150 mg (one 150 mg tablet) PO b.i.d. (without regard to food), if the co-administered PI was RTV-boosted Lopinavir, RTV-boosted Atazanavir, RTV-boosted Saquinavir, RTV-boosted Darunavir
- Maraviroc 300 mg (two 150 mg tablets) PO b.i.d. (without regard to food), if the co-administered PI was Fosamprenavir or Tipranavir

Investigational medicinal product name	Raltegravir
Investigational medicinal product code	J05AX08
Other name	Isentress
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosing of antiretrovirals including study drugs Raltegravir was according to standard dosing as outlined in respective product informations:
- Raltegravir 400 mg (one 400 mg tablet) PO b.i.d. (without regard to food).

Arm title	PHI-group

Arm description:

Patients with primary HIV infection (PHI) (see also "Eligibility") are immediately treated with 2 NRTI + 1 PI/r + Maraviroc + Raltegravir
PHI-patients: Treatment initiation with multi drug class (MDC) HAART.
Therapy: 2 NRTI + 1 PI/r + Maraviroc + Raltegravir

Arm type	Experimental
Investigational medicinal product name	Maraviroc
Investigational medicinal product code	J05AX09
Other name	Celsentri
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosing of antiretrovirals including study drug Maraviroc was according to standard dosing as outlined in respective product informations:
- Maraviroc 150 mg (one 150 mg tablet) PO b.i.d. (without regard to food), if the co-administered PI was RTV-boosted Lopinavir, RTV-boosted Atazanavir, RTV-boosted Saquinavir, RTV-boosted Darunavir
- Maraviroc 300 mg (two 150 mg tablets) PO b.i.d. (without regard to food), if the co-administered PI was Fosamprenavir or Tipranavir

Investigational medicinal product name	Raltegravir
Investigational medicinal product code	J05AX08
Other name	Isentress
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosing of antiretrovirals including study drugs Raltegravir was according to standard dosing as outlined in respective product informations:
- Raltegravir 400 mg (one 400 mg tablet) PO b.i.d. (without regard to food).

Number of subjects in period 1[1]	CHI-group	PHI-group
Started	20	22
Completed	15	16
Not completed	5	6
Consent withdrawn by subject	2	4
Pregnancy	1	-
Relocation abroad	1	1
Unable to visit study center	1	-
Lack of efficacy	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Overall 47 patients signed informed consent, of which five patients turned out to be screening failures due to nonfulfillment of the eligibility criteria (tropism test showed X4 tropism in three patients or Western blot bands >2 in two patients). The safety data are described for N=47 patients.
The efficacy dataset (efficacy population) is based on patients who were enrolled in the study, received at least one dose of study drugs and met the inclusion criteria (N=42 pts.).

Baseline characteristics

Reporting groups	
Reporting group title	CHI-group
Reporting group description:	
Patients with chronic HIV infection (CHI) and with suppressed plasma viral load for at least three years under continuous HAART (Highly active antiretroviral treatment) consisting of 2 NRTI + 1 PI/r (see also "Eligibility") intensified by Maraviroc + Raltegravir CHI-patients: Treatment intensification of PI-based HAART with Maraviroc and Raltegravir. Therapy: 2 NRTI + 1 PI/r + Maraviroc + Raltegravir	
Reporting group title	PHI-group
Reporting group description:	
Patients with primary HIV infection (PHI) (see also "Eligibility") are immediately treated with 2 NRTI + 1 PI/r + Maraviroc + Raltegravir PHI-patients: Treatment initiation with multi drug class (MDC) HAART. Therapy: 2 NRTI + 1 PI/r + Maraviroc + Raltegravir	

Reporting group values	CHI-group	PHI-group	Total
Number of subjects	20	22	42
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)	20	22	42
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	43.3	40.2	
inter-quartile range (Q1-Q3)	33.8 to 51.0	29.4 to 42.7	-
Gender categorical Units: Subjects			
Female	6	1	7
Male	14	21	35
HIV DNA in PBMC (peripheral blood mononuclear cells)			
Measure Analysis Population Description: One Patient of CHI-Group had no HIV DNA measurement.			
Units: log copies/10exp6 PBMC			
median	2.5	3.6	
inter-quartile range (Q1-Q3)	0.2 to 2.7	3.5 to 3.8	-
HIV DNA in CD4+T cells			
Measure Analysis Population Description: One Patient of CHI-Group had no HIV DNA measurement.			
Units: log copies/10exp6 CD4+T cells			
median	3	4.4	
inter-quartile range (Q1-Q3)	2.6 to 3.3	4.1 to 4.6	-
HIV RNA in Plasma			

Measure Description: For PHI-Group HIV RNA at Baseline was measured by Standard Assay. For CHI-Group HIV RNA at Baseline was measured by Single Copy Assay. Measurements between both Groups not comparable (NA) Measure Analysis Population Description: Two Patients of CHI-Group had no single copy measurement.			
Units: log copies/ml			
median	0.3	6.2	
inter-quartile range (Q1-Q3)	0.2 to 0.5	5.3 to 6.9	-
Absolute CD4+T cells			
Units: cells/µl			
median	763	485	
inter-quartile range (Q1-Q3)	555 to 1065	393 to 577	-
Relative CD4+T cells			
Units: percent			
median	33	24	
inter-quartile range (Q1-Q3)	29 to 44	17 to 27	-
CD4+T/CD8+T ratio			
Measure Analysis Population Description: One Patient had no measurement of CD8+T cells .			
Units: units on a scale			
median	0.9	0.4	
inter-quartile range (Q1-Q3)	0.6 to 1.3	0.3 to 0.6	-
Absolute CD8+T cells			
Measure Analysis Population Description: One Patient had no measurement of CD8+T cells.			
Units: cells/µl			
median	864	1117	
inter-quartile range (Q1-Q3)	782 to 1132	836 to 1615	-
Relative CD8+T cells			
Units: percent			
median	39	55	
inter-quartile range (Q1-Q3)	34 to 47	44 to 64	-
Absolute CD8+/CD38+ cells			
Measure Analysis Population Description: Not all patients had a value for this measurement.			
Units: cells/µl			
median	104	872	
inter-quartile range (Q1-Q3)	66 to 160	506 to 1555	-
Relative CD8+/CD38+ cells			
Measure Analysis Population Description: Not all patients had a value for this measurement.			
Units: percent			
median	14	89.9	
inter-quartile range (Q1-Q3)	3.7 to 17	85 to 94	-

Subject analysis sets

Subject analysis set title	Efficacy dataset
Subject analysis set type	Per protocol

Subject analysis set description:

The “efficacy dataset” (efficacy population) was based on patients who were enrolled in the study, received at least one dose of study drugs and met the inclusion criteria.

Subject analysis set title	Safety Analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety dataset (safety population) is based on all patients enrolled in the study and having received at least one dose of study drugs, i.e. 42 eligible patients enrolled in the study (=efficacy dataset), and in addition 5 patients with primary HIV infection, who immediately started on study drugs (as defined by the study protocol) but turned out to be screening failures upon laboratory findings. The count of

patients differed between both datasets (safety dataset N=47; CHI N=20, PHI N=27).

Reporting group values	Efficacy dataset	Safety Analysis set	
Number of subjects	42	47	
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)	42		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
median	41.0		
inter-quartile range (Q1-Q3)	31.7 to 46.3		
Gender categorical Units: Subjects			
Female	7		
Male	35		
HIV DNA in PBMC (peripheral blood mononuclear cells)			
Measure Analysis Population Description: One Patient of CHI-Group had no HIV DNA measurement.			
Units: log copies/10exp6 PBMC			
median	3		
inter-quartile range (Q1-Q3)	2.5 to 3.6		
HIV DNA in CD4+T cells			
Measure Analysis Population Description: One Patient of CHI-Group had no HIV DNA measurement.			
Units: log copies/10exp6 CD4+T cells			
median	3.6		
inter-quartile range (Q1-Q3)	3.1 to 4.4		
HIV RNA in Plasma			
Measure Description: For PHI-Group HIV RNA at Baseline was measured by Standard Assay. For CHI-Group HIV RNA at Baseline was measured by Single Copy Assay. Measurements between both Groups not comparable (NA) Measure Analysis Population Description: Two Patients of CHI-Group had no single copy measurement.			
Units: log copies/ml			
median	NA		
inter-quartile range (Q1-Q3)	NA to NA		
Absolute CD4+T cells Units: cells/µl			
median	570		
inter-quartile range (Q1-Q3)	453 to 766		
Relative CD4+T cells Units: percent			
median	28		
inter-quartile range (Q1-Q3)	23 to 36		

CD4+T/CD8+T ratio			
Measure Analysis Population Description: One Patient had no measurement of CD8+T cells .			
Units: units on a scale			
median	0.6		
inter-quartile range (Q1-Q3)	0.4 to 0.9		
Absolute CD8+T cells			
Measure Analysis Population Description: One Patient had no measurement of CD8+T cells.			
Units: cells/µl			
median	975		
inter-quartile range (Q1-Q3)	790 to 1268		
Relative CD8+T cells			
Units: percent			
median	46		
inter-quartile range (Q1-Q3)	36 to 56		
Absolute CD8+/CD38+ cells			
Measure Analysis Population Description: Not all patients had a value for this measurement.			
Units: cells/µl			
median	204		
inter-quartile range (Q1-Q3)	104 to 870		
Relative CD8+/CD38+ cells			
Measure Analysis Population Description: Not all patients had a value for this measurement.			
Units: percent			
median	33		
inter-quartile range (Q1-Q3)	14 to 89		

End points

End points reporting groups

Reporting group title	CHI-group

Reporting group description:

Patients with chronic HIV infection (CHI) and with suppressed plasma viral load for at least three years under continuous HAART (Highly active antiretroviral treatment) consisting of 2 NRTI + 1 PI/r (see also "Eligibility") intensified by Maraviroc + Raltegravir
CHI-patients: Treatment intensification of PI-based HAART with Maraviroc and Raltegravir.
Therapy: 2 NRTI + 1 PI/r + Maraviroc + Raltegravir

Reporting group title	PHI-group

Reporting group description:

Patients with primary HIV infection (PHI) (see also "Eligibility") are immediately treated with 2 NRTI + 1 PI/r + Maraviroc + Raltegravir
PHI-patients: Treatment initiation with multi drug class (MDC) HAART.
Therapy: 2 NRTI + 1 PI/r + Maraviroc + Raltegravir

Subject analysis set title	Efficacy dataset
Subject analysis set type	Per protocol

Subject analysis set description:

The “efficacy dataset” (efficacy population) was based on patients who were enrolled in the study, received at least one dose of study drugs and met the inclusion criteria.

Subject analysis set title	Safety Analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety dataset (safety population) is based on all patients enrolled in the study and having received at least one dose of study drugs, i.e. 42 eligible patients enrolled in the study (=efficacy dataset), and in addition 5 patients with primary HIV infection, who immediately started on study drugs (as defined by the study protocol) but turned out to be screening failures upon laboratory findings. The count of patients differed between both datasets (safety dataset N=47; CHI N=20, PHI N=27).

Primary: Combined Endpoint Including HIV RNA and HIV DNA

End point title	Combined Endpoint Including HIV RNA and HIV DNA[1]

End point description:

The primary outcome measure (i.e. achievement of 'eradication') is a combined endpoint including cell-associated proviral DNA and plasma HIV RNA and is defined as undetectable cell-associated HIV DNA (copies per 10exp6 PBMC (peripheral blood mononuclear cells) and per 10exp6 CD4 cells) for at least 2 years (measurement by the French ANRS Group) combined with plasma viral load < 50 copies/ml for at least 5 years and undetectable plasma viral load (HIV RNA < 1 copy/ml, 1-copy assay) for at least 2 years.

End point type	Primary

End point timeframe:

Screening, month -3 (= pre-baseline only for CHI-patients), baseline, months 1, 3, 6 and then every 6 months until month 84

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: The primary outcome measure is a combined endpoint including cell-associated proviral DNA and plasma HIV RNA and is defined as undetectable cell-associated HIV DNA (copies per 10exp6 PBMC (peripheral blood mononuclear cells) and per 10exp6 CD4 cells) for at least 2 years combined with plasma viral load < 50 copies/ml for at least 5 years and undetectable plasma viral load (HIV RNA < 1 copy/ml, 1-copy assay) for at least 2 years. None of the patients reached that endpoint.

End point values	CHI-group	PHI-group	Efficacy dataset	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	22	42	
Units: Percent				
Primary outcome measure	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in HIV DNA in PBMC

End point title	Mean Change in HIV DNA in PBMC

End point description:

Mean changes (CI=95% Confidence Intervall) in HIV DNA copies/10exp6 PBMC (= peripheral blood mononuclear cells) from baseline, to evaluate the decay rates of latently infected cell reservoir.

End point type	Secondary

End point timeframe:

Changes from baseline at months 36 and 84

End point values	CHI-group	PHI-group	Efficacy dataset	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20[2]	22[3]	42[4]	
Units: log copies/10exp6 PBMC				
log mean (confidence interval 95%)				
Month 36	0.2 (0.0 to 0.4)	-1.4 (-1.7 to -1.1)	-0.6 (-0.9 to -0.3)	
Month 84	0.1 (-0.1 to 0.3)	-1.3 (-1.6 to -1.0)	-0.6 (-0.9 to -0.3)	

Notes:

[2] - Month 36 N=17 participants
Month 84 N=14 participants

[3] - Month 36 N= 18 participants
Month 84 N= 15 participants

[4] - Month 36 N= 35 participants
Month 84 N= 29 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in HIV DNA in CD4+T cells

End point title	Mean Change in HIV DNA in CD4+T cells

End point description:

Mean change (CI=95% Confidence Intervall) in HIV DNA copies/10exp6 CD4+T cells from baseline, to evaluate the decay rates of latently infected cell reservoir.

End point type	Secondary

End point timeframe:

Change from baseline at months 36 and 84

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[5]	22[6]		
Units: log copies/10exp6 CD4+T cells				
log mean (confidence interval 95%)				
Month 36	0.2 (0.0 to 0.4)	-1.7 (-2.0 to -1.5)		
Month 84	0.2 (-0.0 to 0.3)	-1.7 (-2.0 to -1.4)		

Notes:

[5] - Month 36 N=17 participants
Month 84 N=14 participants
[6] - Month 36 N= 18 participants
Month 84 N= 15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: HIV RNA <50 Copies/ml

End point title	HIV RNA <50 Copies/ml

End point description:

Count of patients with Plasma HIV RNA <50 copies/ml at Month 36 and Month 84.

End point type	Secondary

End point timeframe:

Month 36 and Month 84

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[7]	22[8]		
Units: Count				
Baseline	20	0		
Month 36	19	18		
Month 84	14	14		

Notes:

[7] - Month 36 N=19/19 (100%)
Month 84 N=14/15 (93,3%)
[8] - Month 36 N=18/18 (100%)
Month 84 N=14/15 (93,3%)

Statistical analyses

No statistical analyses for this end point

Secondary: Median change in absolute CD4+T cells

End point title	Median change in absolute CD4+T cells
End point description:	
Median Change from baseline (IQR, interquartile range) in absolute CD4+T cells/µl.	
End point type	Secondary
End point timeframe:	
Month 36 and Month 84	

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[9]	22[10]		
Units: Cells/µl				
median (inter-quartile range (Q1-Q3))				
Month 36	45 (-19 to 150)	395 (192 to 678)		
Month 84	49 (-142 to 180)	457 (242 to 578)		

Notes:

[9] - Month 36 N=19 participants
Month 84 N=15 participants

[10] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Median change in absolute CD8+T cells

End point title	Median change in absolute CD8+T cells
End point description:	
Median Change from baseline (IQR, interquartile range) in absolute CD8+T cells/µl.	
End point type	Secondary
End point timeframe:	
Month 36 and Month 84	

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[11]	22[12]		
Units: Cells/µl				
median (inter-quartile range (Q1-Q3))				
Month 36	170.0 (41.0 to 350.0)	-456.0 (-826.0 to -310.0)		
Month 84	35.0 (-161.0 to 143)	-443.0 (-1670.0 to -185.0)		

Notes:

[11] - Month 36 N=19 participants
Month 84 N=15 participants

[12] - Month 36 N=17 participants
Month 84 N=14 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Median change in CD4+/CD8+ ratio

End point title	Median change in CD4+/CD8+ ratio

End point description:

Median change in CD4+/ CD8+ ratio from baseline (IQR, interquartile range)

End point type	Secondary

End point timeframe:

Month 36 and Month 84

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[13]	22[14]		
Units: Ratio				
median (inter-quartile range (Q1-Q3))				
Month 36	-0.0 (-0.3 to 0.1)	1.0 (0.8 to 1.2)		
Month 84	0.1 (-0.2 to 0.1)	0.9 (0.7 to 1.8)		

Notes:

[13] - Month 36 N=19 participants
Month 84 N=15 participants

[14] - Month 36 N=17 participants
Month 84 N=14 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Median Change in HIV DNA in PBMC

End point title	Median Change in HIV DNA in PBMC

End point description:

Median Change from baseline (IQR, interquartile range) in HIV DNA copies/10exp6 PBMC (= peripheral blood mononuclear cells), to evaluate the decay rates of latently infected cell reservoir.

End point type	Secondary

End point timeframe:

Month 36 and month 84

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[15]	22[16]		
Units: log copies/10exp6 PBMC				
median (inter-quartile range (Q1-Q3))				
Month 36	0.2 (-0.1 to 0.4)	-1.4 (-1.8 to -1.0)		
Month 84	0.0 (-0.1 to 0.4)	-1.4 (-1.8 to -0.8)		

Notes:

[15] - Month 36 N=17 participants
Month 84 N=14 participants

[16] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Median change in HIV DNA in CD4+T cells

End point title	Median change in HIV DNA in CD4+T cells

End point description:

Median Change from baseline (IQR, interquartile range) in HIV DNA in CD4+T cells, to evaluate the decay rates of latently infected cell reservoir.

End point type	Secondary

End point timeframe:

Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[17]	22[18]		
Units: log copies/10^6 CD4+T cells				
median (inter-quartile range (Q1-Q3))				
Month 36	0.1 (-0.0 to 0.4)	-1.7 (-2.1 to -1.3)		
Month 84	0.1 (-0.1 to 0.4)	-1.7 (-2.2 to -1.4)		

Notes:

[17] - Month 36 N=17 participants
Month 84 N=14 participants

[18] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Median change in relative CD4+T cells

End point title	Median change in relative CD4+T cells

End point description:

Median Change from baseline (IQR, interquartile range) in relative CD4+T cells/µl.

End point type	Secondary

End point timeframe:

Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[19]	22[20]		
Units: percentage of Lymphocytes				
median (inter-quartile range (Q1-Q3))				
Month 36	-0.6 (-4.0 to 2.0)	19 (13.0 to 25.0)		
Month 84	0 (-6.1 to 5.0)	22 (11.0 to 31.0)		

Notes:

[19] - Month 36 N=19 participants
Month 84 N=15 participants

[20] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Median Change in absolute CD8+CD38+T cells

End point title	Median Change in absolute CD8+CD38+T cells

End point description:

Median Change from baseline (IQR, interquartile range) in absolute CD8+CD38+T cells/µl.

End point type	Secondary

End point timeframe:

Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[21]	22[22]		
Units: cells/µl				
median (inter-quartile range (Q1-Q3))				
Month 36	11 (-32 to 73)	-1077 (-2170 to -500)		
Month 84	-22.5 (-82 to 17.9)	-1201.5 (-2454 to -621)		

Notes:

[21] - Month 36 N=13 participants
Month 84 N=10 participants

[22] - Month 36 N= 9 participants
Month 84 N= 8 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute HIV DNA in PBMC

End point title	Absolute HIV DNA in PBMC

End point description:

Absolute HIV DNA in PBMC (= peripheral blood mononuclear cells) at baseline and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[23]	22[24]		
Units: log copies/10^6 PBMC				
median (inter-quartile range (Q1-Q3))				
Month 36	2.7 (2.5 to 2.8)	2.2 (1.9 to 2.3)		
Month 84	2.4 (2.4 to 2.8)	2.3 (2.0 to 2.6)		
Baseline	2.5 (2.0 to 2.7)	3.6 (3.5 to 3.8)		

Notes:

[23] - Month 36 N=17 participants
Month 84 N=15 participants

[24] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute HIV DNA in CD4+T cells

End point title	Absolute HIV DNA in CD4+T cells

End point description:

Absolute HIV DNA in CD4+T cells at baseline and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[25]	22[26]		
Units: log copies/10^6 CD4+T cells				
median (inter-quartile range (Q1-Q3))				
Month 36	3.2 (3.0 to 3.4)	2.7 (2.4 to 2.8)		
Month 84	3.1 (2.9 to 3.4)	2.7 (2.3 to 3.1)		
Baseline	3.0 (2.6 to 3.3)	4.4 (4.1 to 4.6)		

Notes:

[25] - Month 36 N=17 participants
Month 84 N=15 participants
Baseline N= 19 participants
[26] - Month 36 N=18 participants
Month 84 N=15 participants
Baseline N=22 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute CD4+T cells

End point title	Absolute CD4+T cells

End point description:

Absolute CD4+T cells at baseline and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[27]	22[28]		
Units: cells/µl				
median (inter-quartile range (Q1-Q3))				
Month 36	827 (565 to 1145)	915.5 (638 to 1179)		
Month 84	733 (545 to 964)	938 (739 to 1164)		
Baseline	762.5 (554 to 1065)	484.5 (393 to 577)		

Notes:

[27] - Month 36 N=19 participants
Month 84 N=15 participants

[28] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Relative CD4+ T cells

End point title	Relative CD4+ T cells

End point description:

Relative CD4+T cells at baseline and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[29]	22[30]		
Units: percentage of Lymphocytes				
median (inter-quartile range (Q1-Q3))				
Baseline	32.5 (28.5 to 43.5)	24.0 (17.0 to 27.0)		
Month 36	33.0 (28.0 to 43.6)	41.0 (38.0 to 46.0)		
Month 84	32.0 (24.0 to 39.0)	43.0 (36.6 to 48.0)		

Notes:

[29] - Month 36 N=19 participants
Month 84 N=15 participants
Baseline N=19

[30] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+/CD8+ Ratio

End point title	CD4+/CD8+ Ratio

End point description:

Median CD4+/CD8+ ratio at baseline (IQR, interquartile range) and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[31]	22[32]		
Units: ratio				
median (inter-quartile range (Q1-Q3))				
Baseline	0.9 (0.6 to 1.3)	0.4 (0.3 to 0.6)		
Monrth 36	0.8 (0.6 to 1.1)	1.3 (1.1 to 1.9)		
Month 84	0.7 (0.5 to 1.0)	1.4 (1.0 to 2.1)		

Notes:

[31] - Month 36 N=19 participants
Month 84 N=15 participants

[32] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute CD8+T cells

End point title	Absolute CD8+T cells

End point description:

Median CD8+T cells/µl at baseline and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[33]	22[34]		
Units: cells/µl				
median (inter-quartile range (Q1-Q3))				
Baseline	864 (782 to 1132)	1117 (836 to 1615)		
Month 36	1010 (858 to 1330)	589 (466 to 851)		
Month 84	1000 (820 to 1189)	692 (511 to 825)		

Notes:

[33] - Month 36 N=19 participants
Month 84 N=15 participants

[34] - Month 36 N=18 participants
Month 84 N=15 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute CD8+CD38+T cells

End point title	Absolute CD8+CD38+T cells

End point description:

Absolute CD8+CD38+T cells/µl at baseline and during follow-up at month 36 and 84 (IQR, interquartile range).

End point type	Secondary

End point timeframe:

Baseline, Month 36 and month 84.

End point values	CHI-group	PHI-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[35]	22[36]		
Units: cells/µl				
median (inter-quartile range (Q1-Q3))				
Baseline	104 (66 to 160)	871.5 (506 to 1555)		
Month 36	163 (63 to 191)	79 (12 to 121)		
Month 84	120 (48 to 170)	64 (37 to 156)		

Notes:

[35] - Baseline N=15 participants
Month 36 N=17 participants
Month 84 N=14 participants

[36] - Baseline N=14 participants
Month 36 N=15 participants
Month 84 N=13 participants

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the course of the study, the adverse events were reported over all patients who started with study drugs (N=47, safety population) at every patient visit, including events occurring during post-follow-up observation period.

Adverse event reporting additional description:

The safety dataset (safety population) is based on all patients enrolled in the study and having received at least one dose of study drugs (N=47 patients).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	CHI group

Reporting group description: -

Reporting group title	PHI-group

Reporting group description: -

Serious adverse events	CHI group	PHI-group	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)	8 / 27 (29.63%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			

subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture follow-up	Additional description: Follow-up		
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism arterial			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia stroke			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Renal stone removal			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia repair			

subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leg amputation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion induced			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal stone removal follow-up			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal prolapse			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			

subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Burnout syndrome			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary	Additional description: Hospitalization due to suspected urolithiasis (not confirmed)		
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Rectal abscess			
subjects affected / exposed	0 / 20 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CHI group	PHI-group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	26 / 27 (96.30%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 20 (10.00%)	5 / 27 (18.52%)	
occurrences (all)	6	6	
Oedema peripheral			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 20 (15.00%)	2 / 27 (7.41%)	
occurrences (all)	4	2	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 20 (15.00%)	6 / 27 (22.22%)	
occurrences (all)	4	7	
Sleep disorder			
subjects affected / exposed	4 / 20 (20.00%)	3 / 27 (11.11%)	
occurrences (all)	4	3	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			

Concussion			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Contusion			
subjects affected / exposed	3 / 20 (15.00%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 20 (15.00%)	0 / 27 (0.00%)	
occurrences (all)	4	0	
Headache			
subjects affected / exposed	0 / 20 (0.00%)	4 / 27 (14.81%)	
occurrences (all)	0	6	
Paraesthesia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	4	
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Abdominal tenderness			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Anal fissure			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	8 / 20 (40.00%)	10 / 27 (37.04%)	
occurrences (all)	9	20	
Dysphagia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Enteritis			

subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Flatulence			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Haemorrhoids			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	3	
Nausea			
subjects affected / exposed	4 / 20 (20.00%)	3 / 27 (11.11%)	
occurrences (all)	4	4	
Proctalgia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Proctitis			
subjects affected / exposed	0 / 20 (0.00%)	4 / 27 (14.81%)	
occurrences (all)	0	4	
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
Ocular icterus			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	3	
Alopecia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Night sweats			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Pruritus			

subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	4	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 20 (15.00%)	0 / 27 (0.00%)	
occurrences (all)	6	0	
Back pain			
subjects affected / exposed	2 / 20 (10.00%)	6 / 27 (22.22%)	
occurrences (all)	2	6	
Musculoskeletal pain			
subjects affected / exposed	3 / 20 (15.00%)	0 / 27 (0.00%)	
occurrences (all)	4	0	
Myalgia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Osteoarthritis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	2 / 27 (7.41%)	
occurrences (all)	2	3	
Spinal pain			
subjects affected / exposed	0 / 20 (0.00%)	4 / 27 (14.81%)	
occurrences (all)	0	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 20 (55.00%)	14 / 27 (51.85%)	
occurrences (all)	26	30	
Acute hepatitis C			

subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Anal abscess			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Anal chlamydia infection			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Epididymitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Folliculitis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	4	
Gastrointestinal viral infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Gingivitis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	3	
Gonorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	3	
Herpes virus infection			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	3	
Herpes zoster			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Oral herpes			
subjects affected / exposed	0 / 20 (0.00%)	4 / 27 (14.81%)	
occurrences (all)	0	4	
Otitis media			

subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	4	
Sinusitis			
subjects affected / exposed	4 / 20 (20.00%)	3 / 27 (11.11%)	
occurrences (all)	5	4	
Syphilis			
subjects affected / exposed	3 / 20 (15.00%)	8 / 27 (29.63%)	
occurrences (all)	9	11	
Tonsillitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	4	0	
Urethritis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Urethritis gonococcal			
subjects affected / exposed	0 / 20 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Bronchitis			
subjects affected / exposed	4 / 20 (20.00%)	5 / 27 (18.52%)	
occurrences (all)	7	6	
Chlamydial infection			
subjects affected / exposed	0 / 20 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	7 / 20 (35.00%)	4 / 27 (14.81%)	
occurrences (all)	8	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2015	The New Era Study is an ongoing prospective 7-year clinical trial initiated in 2009 using 5-drug cART (combination antiretroviral therapy) in patients with primary HIV infection (PHI, ≤2 Western blot bands) and in patients with chronic HIV-infection on suppressive PI-based HAART for ≥3 years without prior virologic failure (CHI). The primary objectives of the study were to halt residual viral replication in plasma and to achieve depletion of cell-associated HIV-DNA ('proviral DNA') as a step towards (functional) HIV cure which could be proven by treatment interruption. The primary and secondary outcome measures of the New Era Study are cell-associated HIV-DNA copies per 10exp6 peripheral blood mononuclear cells (PBMC), plasma HIV-RNA level, absolute and relative CD4+ and CD8+ T-cell counts, CD4/CD8 ratio, and CD8+CD38+ T-cell count. The implementation of Amendment 1.0 comprising the measurement of additional laboratory parameters does not affect primary objectives but secondary objectives are amended. The rationale for amending additional laboratory markers to be measured is based on new questions arising from intensified worldwide cure research since the beginning of the New Era Study. According to the study protocol, treatment can be interrupted in case of plasma HIV-RNA <50 cop./ml for ≥5 years, undetectable HIV-RNA using single-copy assay for ≥2 years coupled with undetectable proviral DNA levels in PBMC for ≥2 years. As shown by the Visconti post-treatment controllers and other case reports of post treatment controlling (PTC) further virologic, immunologic and genetic markers are needed to better predict virus control after treatment interruption (Saez-Cirion 2013). Therefore, the measurement of laboratory parameters (one additional blood sampling per patient) will be extended in the population of the New Era Study in order to better characterize and discriminate these patients in terms of immunologic and virologic parameters.

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/29760693

http://www.ncbi.nlm.nih.gov/pubmed/1252566

http://www.ncbi.nlm.nih.gov/pubmed/1609929

http://www.ncbi.nlm.nih.gov/pubmed/10613829

http://www.ncbi.nlm.nih.gov/pubmed/17784786

http://www.ncbi.nlm.nih.gov/pubmed/18171475

http://www.ncbi.nlm.nih.gov/pubmed/12754504

http://www.ncbi.nlm.nih.gov/pubmed/10341272

http://www.ncbi.nlm.nih.gov/pubmed/25047577

http://www.ncbi.nlm.nih.gov/pubmed/21552772

http://www.ncbi.nlm.nih.gov/pubmed/24152233

http://www.ncbi.nlm.nih.gov/pubmed/23516360