ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 07/22/2015

ClinicalTrials.gov ID: NCT00487188

Study Identification

Unique Protocol ID:	MV18406
Brief Title:	A Study to Evaluate the Safety and Efficacy of Adding Enfuvirtide to Oral Highly Active Antiretroviral Therapy (HAART) in Human Immunodeficiency Virus (HIV) Patients With Prior Treatment Experience (INTENSE)
Official Title:	Phase IIIb/IV Randomized, Controlled Study Evaluating an Intensification Treatment Strategy of Adding Enfuvirtide (ENF) to an Oral Highly Active AntiRetroviral Therapy (HAART) in Treatment Experienced Patients
Secondary IDs:	

Study Status

Record Verification:	July 2015
Overall Status:	Completed
Study Start:	November 2005
Primary Completion:	November 2007 [Actual]
Study Completion:	April 2008 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: AC-05-027 Board Name: Comite Etico de Investigacion Clinica del Hospital Universitario Germans Trias i Pujol Board Affiliation: Unknown Phone: +34934978956 Email: ciec.germanstrias@gencat.net
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Spain: Agency of Medicines

Study Description

Brief Summary: To assess the efficacy of enfuvirtide (Fuzeon) added to HAART compared to treatment with HAART alone in achieving and maintaining viral load suppression.

Detailed Description: This study consisted of two phases. In the Induction phase patients were randomized at Baseline 1 (BL1) in a 1:2 ratio to receive:

- I1: HAART or
- I2: Enfuvirtide (90 mg twice a day) + HAART.

Participants who achieved viral suppression < 50 copies/mL by week 24, confirmed by week 28 or earlier, qualified to enter the Maintenance Phase which started at Baseline 2 (BL2), four weeks after confirmation of response. The Maintenance Phase consisted of three treatment groups:

- M1: HAART continued (patients from I1)

Patients on ENF+HAART (I2) were re-randomized (at a 1:1 ratio) at BL2 to:

- M2: Enfuvirtide stopped and HAART continued
- M3: Enfuvirtide + HAART continued.

The duration of the Maintenance Phase was from BL2 up to 48 weeks after BL1. BL2 could start at the earliest at Week 12 and at the latest Week 32.

Conditions

Conditions:	HIV Infections
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	47 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: ENF + HAART Participants received Enfuvirtide (ENF) 90 mg administered by subcutaneous injection twice a day for up to 48 weeks in addition to an oral highly active antiretroviral treatment (HAART) regimen for up to 48 weeks.	Drug: Enfuvirtide 90 mg subcutaneous injection twice a day Other Names: • Fuzeon Drug: Highly active antiretroviral treatment (HAART) An oral HAART regimen of 3-5 antiretrovirals was chosen by the physician and patient, based on the patient's prior treatment history and genotypic antiretroviral resistance testing.
Active Comparator: HAART Participants received an oral highly active antiretroviral treatment (HAART) regimen, consisting of 3-5 antivirals for up to 48 weeks.	Drug: Highly active antiretroviral treatment (HAART) An oral HAART regimen of 3-5 antiretrovirals was chosen by the physician and patient, based on the patient's prior treatment history and genotypic antiretroviral resistance testing.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- HIV-1 infected adults >=18 years of age;
- currently on antiretroviral (ARV) therapy;
- previously treated with 2 or 3 different antiretroviral classes;
- HIV-1 Ribonucleic acid (RNA) >=1,000 copies/mL;
- Cluster differentiation antigen four (CD4) lymphocyte count >=200 cells/mm^3;
- females of childbearing potential must be willing to use a reliable form of effective barrier contraception for the duration of the study and for 30 days after the last dose of study drug.

Exclusion Criteria:

- history of prior use of enfuvirtide or T-1249;
- women who are pregnant, breastfeeding or planning to become pregnant during the study;
- active, untreated opportunistic infection;
- patients on treatment interruption, or patients interrupting ARV therapy within 4 weeks of screening or during the screening period for reasons either than toxicity management.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
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Locations: France
Paris, France, 75018

Nantes, France, 44035

Netherlands
Amsterdam, Netherlands, 1105 AZ

Tilburg, Netherlands, 5022 GC

Germany
Frankfurt Am Main, Germany, 60596

Erlangen, Germany, 91054

Bonn, Germany, 53127

France

Le Kremlin-bicetre, France, 94275

Switzerland
Zürich, Switzerland, 8091

Italy
Brescia, Italy, 25123

Milano, Italy, 20157

Milano, Italy, 20157

Milano, Italy, 20157

Bari, Italy, 70100

Roma, Italy, 00185

Roma, Italy, 00149

Bagno A Ripoli, Italy, 50011

Spain
Cádiz, Spain, 11009

Malaga, Spain, 29010

Barcelona, Spain, 08370

Huelva, Spain, 21005

Córdoba, Spain, 14004

San Sebastian, Spain, 20014

Sevilla, Spain, 41013

Madrid, Spain, 28046

Madrid, Spain, 28041

Madrid, Spain, 28041

Madrid, Spain, 28034

Barcelona, Spain, 08036

Barcelona, Spain, 08901

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Valencia, Spain, 46014

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Mexico City, Mexico, 14000

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Cleveland, Ohio, United States, 44109

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Dallas, Texas, United States, 75246

Austin, Texas, United States, 78705

France
Poitiers, France, 86021

Israel
Ramat Gan, Israel, 52662

France
Villeneuve-sur-lot, France, 47307

Italy
Milano, Italy, 20127

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	A total of 47 patients were enrolled into the study at 20 investigational sites in France, Italy, Spain, Mexico, Germany and the US. Study starting 15NOV2005 and ending 5NOV2007.
Pre-Assignment Details	In the Induction Phase participants were randomized (2:1 ratio) to receive ENF + HAART or HAART. In the Maintenance Phase participants in the HAART group who responded (viral load < 50 copies/mL) continued to receive HAART; those who responded in the ENF + HAART group were re-randomized (1:1 ratio) to receive ENF + HAART or HAART (ENF removed).

Reporting Groups

	Description
ENF + HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment during the Induction and Maintenance Phase for up to 48 weeks of treatment.
HAART	Participants received highly active antiretroviral treatment during the Induction and Maintenance Phase for up to 48 weeks of treatment.
HAART (ENF Removed)	Participants who had received ENF + HAART during the Induction Phase and responded to treatment by Week 24 continued to receive HAART alone during the Maintenance Phase, for a total of 48 weeks of treatment.

Induction Phase

	ENF + HAART	HAART	HAART (ENF Removed)
Started	31	16	0 [1]
Safety Population	29	18 [2]	0
Completed	22	9	0
Not Completed	9	7	0
Abnormality of Laboratory Test	0	1	0
Adverse Event	5	0	0
Lack of Efficacy	0	1	0
Protocol Violation	1	0	0
Refused Treatment	1	2	0
Lost to Follow-up	2	2	0
Administrative	0	1	0

[1] Participants were only randomized to this treatment arm in the Maintenance Phase
[2] 2 patients randomized to ENF + HARRT only received treatment with HAART

Maintenance Phase

	ENF + HAART	HAART	HAART (ENF Removed)
Started	10	8	9
Completed	7	8	8
Not Completed	3	0	1
Adverse Event	1	0	0
Death	1	0	0
Lost to Follow-up	1	0	0
Administrative	0	0	1

Baseline Characteristics

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.
HAART	Participants received highly active antiretroviral treatment.

Baseline Measures

	ENF+HAART	HAART	Total
Number of Participants	29	18	47
Age, Continuous [units: years] Mean (Standard Deviation)	44.1 (7.04)	41.9 (10.57)	43.3 (8.52)
Gender, Male/Female [units: participants]			
Female	7	3	10
Male	22	15	37

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With Viral Suppression: HIV-1 RNA < 50 Copies/mL During the Induction Phase
Measure Description	Participants whose viral load achieved suppression (HIV-1 RNA < 50 copies/mL) at Week 24 at the latest, confirmed at Week 28 (2 consecutive assessments ≥ 28 days apart) were defined as responders. Patients who discontinued the study or did not respond to assigned treatment by week 28 were considered as non-responders.
Time Frame	From Baseline 1 to Week 28
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population 1 (ITT1) population (patients evaluable for efficacy in the induction phase)

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.
HAART	Participants received highly active antiretroviral treatment.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	31	16
Number of Participants With Viral Suppression: HIV-1 RNA < 50 Copies/mL During the Induction Phase [units: Participants]	20	8

2. Secondary Outcome Measure:

Measure Title	Time to Achieving HIV-1 RNA < 50 Copies/mL During the Induction Phase
Measure Description	The time to achieving HIV-1 RNA <50 copies/mL was counted from Baseline 1 until the first of the two consecutive <50 copies/mL measurements. Patients who discontinued from the study or patients who did not have confirmed virological response by week 28 were classed as non-responders and censored at Week 24.
Time Frame	Baseline 1 until Week 28.

Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population 1 (ITT1) population (patients evaluable for efficacy in the induction phase).

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.
HAART	Participants received highly active antiretroviral treatment.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	31	16
Time to Achieving HIV-1 RNA < 50 Copies/mL During the Induction Phase [units: days] Median (Inter-Quartile Range)	57.0 (29 to 119)	141.0 (70 to NA) [1]

[1] The 75% quartile could not be calculated as >75% of patients did not achieve HIV-1 RNA < 50 Copies/mL in this arm.

3. Secondary Outcome Measure:

Measure Title	Number of Participants With Viral Suppression HIV-1 RNA < 400 Copies/mL During the Induction Phase
Measure Description	Participants whose viral load achieved suppression (HIV-1 RNA < 400 copies/mL) by Week 24 at the latest, confirmed at Week 28 (2 consecutive assessments ≥ 28 days apart) were defined as responders. Patients who discontinued the study or did not respond to assigned treatment by Week 28 were considered as non-responders.
Time Frame	From Baseline 1 to Week 28
Safety Issue?	No

Analysis Population Description

ITT1 population (patients evaluable for efficacy in the induction phase)

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.

	Description
HAART	Participants received highly active antiretroviral treatment.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	31	16
Number of Participants With Viral Suppression HIV-1 RNA < 400 Copies/mL During the Induction Phase [units: Participants]	21	8

4. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Viral Load
Measure Description	Change from Baseline in log10 HIV-1 RNA at Week 24. Least squares means were calculated from an analysis of covariance (ANCOVA) model with treatment, a flag variable "removed ENF at re-randomization" and Baseline viral load as independent variables.
Time Frame	Baseline and Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population 1 (ITT1) population (patients evaluable for efficacy in the Induction Phase). Baseline values were carried forward (i.e. the change from baseline set to zero) for patients with missing data at week 24 or who withdrew prior to the week 24 time window.

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.
HAART	Participants received highly active antiretroviral treatment.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	31	16
Change From Baseline to Week 24 in Viral Load [units: log10 copies/mL] Least Squares Mean (95% Confidence Interval)	-1.402 (-1.854 to -0.949)	-1.156 (-1.710 to -0.601)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Cluster Differentiation Antigen Four Positive (CD4+) Cell Counts
Measure Description	Change from Baseline in CD4+ Cell Counts at Week 24. Least squares means were calculated from an ANCOVA model with treatment as an independent variable.
Time Frame	Baseline and Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population 1 (ITT1) population (patients evaluable for efficacy in the Induction Phase). Baseline values were carried forward (i.e. the change from baseline set to zero) for patients with missing data at week 24 or who withdrew prior to the week 24 time window.

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.
HAART	Participants received highly active antiretroviral treatment.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	31	16
Change From Baseline to Week 24 in Cluster Differentiation Antigen Four Positive (CD4+) Cell Counts [units: cells/mm^3] Least Squares Mean (95% Confidence Interval)	20.81 (-18.89 to 60.50)	17.88 (-37.38 to 73.13)

6. Secondary Outcome Measure:

Measure Title	Percentage of Induction Phase Participants With Viral Load < 50 Copies/mL at 48 Weeks
Measure Description	The percentage of participants from the Induction Phase who maintained HIV-1 RNA < 50 Copies/mL at Week 48. Patients who discontinued from the study, rebounded to ≥ 50 copies/mL (i.e., had two consecutive readings ≥ 50 copies/mL), had missing data or had virological failure by Week 48 were classed as non-responders.
Time Frame	Week 48

Safety Issue?	No

Analysis Population Description

Induction Phase Intent-to-Treat Population 1 (ITT1).

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide (ENF) 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment (HAART) in the Induction Phase. In the Maintenance Phase, participants either continued to receive ENF+HAART or HAART alone. This group contains all patients who were randomized to ENF+HAART at BL1 and follows the patients throughout 48 weeks, regardless of which arm they were randomized to at BL2.
HAART	Participants received highly active antiretroviral treatment during both the Induction and Maintenance Phase.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	31	16
Percentage of Induction Phase Participants With Viral Load < 50 Copies/mL at 48 Weeks [units: percentage of participants]	45.2	25.0

7. Secondary Outcome Measure:

Measure Title	Percentage of Maintenance Phase Participants With Viral Load < 50 Copies/mL at 48 Weeks
Measure Description	The percentage of participants from the Maintenance Phase who maintained HIV-1 RNA < 50 copies/mL at Week 48. Patients who discontinued from the study, rebounded to ≥ 50 copies/mL (i.e., had two consecutive readings ≥ 50 copies/mL), had missing data or had virological failure by Week 48 were classed as non-responders.
Time Frame	Week 48
Safety Issue?	No

Analysis Population Description

Maintenance Phase Intent-to-Treat Population 2 (ITT2).

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide (ENF) 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment (HAART) in the Induction Phase. In the Maintenance Phase, participants either continued to receive ENF+HAART or HAART alone. This group contains all patients who entered the Maintenance phase from the ENF+HAART Induction phase, regardless of which arm they were randomized to at BL2.
HAART	Participants received highly active antiretroviral treatment during both the Induction and Maintenance Phase.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	19	8
Percentage of Maintenance Phase Participants With Viral Load < 50 Copies/mL at 48 Weeks [units: percentage of participants]	73.7	50.0

8. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 48 in Cluster Differentiation Antigen Four Positive (CD4) Cell Counts
Measure Description	Change from Baseline in CD4 Cell Counts at Week 48. Least squares means were calculated from an ANCOVA model with treatment and baseline CD4 count as independent variables.
Time Frame	Baseline 1 and Week 48
Safety Issue?	No

Analysis Population Description

Intent-to-Treat Population 2 (ITT2) population (patients evaluable for efficacy in the Maintenance Phase). Baseline values were carried forward (i.e. the change from baseline set to zero) for patients with missing data at week 48 or who withdrew prior to the week 48 time window.

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide (ENF) 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment (HAART) in the Induction Phase. In the Maintenance Phase, participants either continued to receive ENF+HAART or HAART alone. This group contains all patients who entered the Maintenance phase from the ENF+HAART Induction phase, regardless of which arm they were randomized to at BL2.

	Description
HAART	Participants received highly active antiretroviral treatment during both the Induction and Maintenance Phase.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	19	8
Change From Baseline to Week 48 in Cluster Differentiation Antigen Four Positive (CD4) Cell Counts [units: cells/mm^3] Least Squares Mean (95% Confidence Interval)	73.09 (-4.10 to 150.28)	50.79 (-68.24 to 169.83)

9. Secondary Outcome Measure:

Measure Title	Time to Loss of Viral Response During the Maintenance Phase
Measure Description	The time to loss of viral response (defined as HIV-1 RNA <50 copies/mL) was counted from Baseline 2 until the first of two consecutive ≥50 copies/mL measurements. Only patients who were qualified for entering the Maintenance Phase were included in the analysis.
Time Frame	From Baseline 2 to Week 48.
Safety Issue?	No

Analysis Population Description

Maintenance Phase Intent-to-Treat Population 2 (ITT2)

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide (ENF) 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment (HAART) in the Induction Phase. In the Maintenance Phase, participants either continued to receive ENF+HAART or HAART alone. This group contains all patients who entered the Maintenance phase from the ENF+HAART Induction phase, regardless of which arm they were randomized to at BL2.
HAART	Participants received highly active antiretroviral treatment during both the Induction and Maintenance Phase.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	19	8
Time to Loss of Viral Response During the Maintenance Phase [units: days] Median (Inter-Quartile Range)	NA (NA to NA) [1]	NA (NA to NA) [2]

[1] Median time to loss of viral response could not be estimated due to the low number of patients with loss of viral response in this arm (4 out of 19 ITT2 patients) and the inter-quartile range was not calculated.

[2] Median time to loss of viral response could not be estimated due to the low number of patients with loss of viral response in this arm (3 out of 8 ITT2 patients) and the inter-quartile range was not calculated.

10. Secondary Outcome Measure:

Measure Title	Time to Virological Failure During the Maintenance Phase
Measure Description	Time to virological failure (defined as HIV-1 RNA ≥ 400 copies/mL) was counted from Baseline 2 until the first of the two consecutive ≥400 copies/mL measurements. Only patients who were qualified for entering the Maintenance Phase were included in the analyses.
Time Frame	From Baseline 2 to Week 48.
Safety Issue?	No

Analysis Population Description

Maintenance Phase Intent-to-Treat Population 2 (ITT2)

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide (ENF) 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment (HAART) in the Induction Phase. In the Maintenance Phase, participants either continued to receive ENF+HAART or HAART alone. This group contains all patients who entered the Maintenance Phase from the ENF+HAART Induction Phase, regardless of which arm they were randomized to at BL2.
HAART	Participants received highly active antiretroviral treatment during both the Induction and Maintenance Phase.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	19	8
Time to Virological Failure During the Maintenance Phase [units: days] Median (Inter-Quartile Range)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] Median time to virological failure could not be estimated due to the low number of patients with virological failure in this arm and the inter-quartile range was not calculated.

11. Secondary Outcome Measure:

Measure Title	Number of Participants With Virological Failure During the Maintenance Phase
Measure Description	Virological failure was defined by 2 consecutive HIV-1 RNA values ≥ 400 copies/mL during the Maintenance Phase.
Time Frame	From Baseline 2 to Week 48.
Safety Issue?	No

Analysis Population Description

Maintenance Phase Intent-to-Treat Population 2 (ITT2)

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide (ENF) 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment (HAART) in the Induction Phase. In the Maintenance Phase, participants either continued to receive ENF+HAART or HAART alone. This group contains all patients who entered the Maintenance Phase from the ENF+HAART Induction Phase, regardless of which arm they were randomized to at BL2.
HAART	Participants received highly active antiretroviral treatment during both the Induction and Maintenance Phase.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	19	8
Number of Participants With Virological Failure During the Maintenance Phase [units: Participants]	3	0

12. Secondary Outcome Measure:

Measure Title	Percentage of Participants Maintaining CD4+ Count During the Maintenance Phase
Measure Description	Maintenance of CD4+ count defined as having greater than or equal to 200 cells/mm^3 at Baseline 2 (BL2) and greater than or equal to 200 cells/mm^3 at Week 48.
Time Frame	Baseline 2 to Week 48.
Safety Issue?	No

Analysis Population Description

Maintenance Phase ITT2 population with a Baseline 2 CD4+ count of greater than or equal to 200 cells/mm^3.

Reporting Groups

	Description
ENF + HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment during the Induction and Maintenance Phase for up to 48 weeks of treatment.
HAART	Participants received highly active antiretroviral treatment during the Induction and Maintenance Phase for up to 48 weeks of treatment.
HAART (ENF Removed)	Participants who had received ENF + HAART during the Induction Phase and responded to treatment by Week 24 continued to receive HAART alone during the Maintenance Phase, for a total of 48 weeks of treatment.

Measured Values

	ENF + HAART	HAART	HAART (ENF Removed)
Number of Participants Analyzed	9	8	8
Percentage of Participants Maintaining CD4+ Count During the Maintenance Phase [units: percentage of participants]			
Week 48 CD4+ Count ≥200 cells/mm^3	66.67	75.00	75.00
Week 48 CD4+ Count Missing	33.33	25.00	12.50

13. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Improvement in CD4+ Count During the Maintenance Phase

Measure Description	Improvement of CD4+ count defined as having from 100 to less than 200 CD4+ cells/mm^3 at Baseline 2 (BL2) and greater than or equal to 200 cells/mm^3 at Week 48.
Time Frame	Baseline 2 to Week 48.
Safety Issue?	No

Analysis Population Description

Maintenance Phase ITT2 population with a Baseline 2 CD4+ count of ≥100 to <200 cells/mm^3.

Reporting Groups

	Description
ENF + HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment during the Induction and Maintenance Phase for up to 48 weeks of treatment.
HAART	Participants received highly active antiretroviral treatment during the Induction and Maintenance Phase for up to 48 weeks of treatment.
HAART (ENF Removed)	Participants who had received ENF + HAART during the Induction Phase and responded to treatment by Week 24 continued to receive HAART alone during the Maintenance Phase, for a total of 48 weeks of treatment.

Measured Values

	ENF + HAART	HAART	HAART (ENF Removed)
Number of Participants Analyzed	1	0	1
Percentage of Participants With Improvement in CD4+ Count During the Maintenance Phase [units: percentage of participants]			
Week 48 CD4+ Count ≥200 cells/mm^3	100.00		100.00
Week 48 CD4+ Count Missing	0		0

14. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AEs) During the Induction Phase
Measure Description	A serious AE (SAE) is an event which: results in death, is life-threatening, disabling or incapacitating; is a congenital anomaly in the offspring of a patient who received study drug; requires or prolongs inpatient hospitalization; jeopardizes the patient or require medical or surgical intervention to prevent one of the outcomes above; any Grade 4 laboratory value considered by the investigator clinically significant or that requires an action; any injection site reaction that meets SAE criteria above. Non-serious AEs reported include pneumonia and non-serious AEs that led to discontinuation.
Time Frame	Start of the study treatment until the end of the Induction Phase (Week 12 to Week 32)

Safety Issue?	No

Analysis Population Description
Safety Population

Reporting Groups

	Description
ENF+HAART	Participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment.
HAART	Participants received highly active antiretroviral treatment.

Measured Values

	ENF+HAART	HAART
Number of Participants Analyzed	29	18
Number of Participants With Adverse Events (AEs) During the Induction Phase [units: participants]		
Serious Adverse Event	3	3
Non-serious Adverse Event	3	1
Adverse Events Leading to Withdrawal	5	1

Reported Adverse Events

Time Frame	From the start of the study treatment until 28 days after the last dose of the study medication.
Additional Description	Per protocol, AEs of pneumonia (non-serious and serious), AEs that lead to discontinuation, and AEs that are serious were reported. Unless fatal, any acquired immunodeficiency syndrome (AIDS)-defining events (ADEs), as defined by the 1993 Center for Disease Control (CDC) AIDS Surveillance Case Definitions, are excluded from the definition of SAE.

Reporting Groups

	Description
Induction: ENF+HAART	During the Induction Phase participants received enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment for a maximum of 32 weeks.

	Description
Induction Phase: HAART	During the Induction Phase participants received highly active antiretroviral treatment for a maximum of 32 weeks.
Maintenance Phase: ENF + HAART	During the Maintenance Phase, participants who had received ENF+HAART and who responded to treatment during the Induction Phase continued to receive enfuvirtide 90 mg subcutaneously twice a day in combination with highly active antiretroviral treatment for up to 48 weeks of total treatment.
Maintenance Phase: HAART (ENF Removed)	During the Maintenance Phase, participants who had received ENF+HAART and who responded to treatment during the Induction Phase continued to receive HAART alone during the Maintenance Phase, for up to a total of 48 weeks treatment.
Maintenance Phase: HAART	During the Maintenance Phase, participants who had received HAART alone and who responded to treatment during the Induction Phase continued to receive highly active antiretroviral treatment for up to 48 weeks of total treatment.

Serious Adverse Events

	Induction: ENF+HAART	Induction Phase: HAART	Maintenance Phase: ENF + HAART	Maintenance Phase: HAART (ENF Removed)	Maintenance Phase: HAART
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	3/29 (10.34%)	3/18 (16.67%)	2/10 (20%)	3/9 (33.33%)	0/8 (0%)
Blood and lymphatic system disorders					
ANAEMIA [A] †	1/29 (3.45%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Gastrointestinal disorders					
ABDOMINAL PAIN [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
VOMITING [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
General disorders					
INJECTION SITE REACTION [A] †	1/29 (3.45%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Hepatobiliary disorders					
HEPATIC FAILURE [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
HEPATIC FUNCTION ABNORMAL [A] †	0/29 (0%)	0/18 (0%)	1/10 (10%)	0/9 (0%)	0/8 (0%)
Infections and infestations					
INFECTION [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)

	Induction: ENF+HAART	Induction Phase: HAART	Maintenance Phase: ENF + HAART	Maintenance Phase: HAART (ENF Removed)	Maintenance Phase: HAART
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
PAROTITIS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
PNEUMONIA [A] †	0/29 (0%)	0/18 (0%)	1/10 (10%)	0/9 (0%)	0/8 (0%)
POSTOPERATIVE WOUND INFECTION [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Musculoskeletal and connective tissue disorders					
RHABDOMYOLYSIS [A] †	1/29 (3.45%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
ANAL CANCER [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)
Renal and urinary disorders					
CALCULUS URETERIC [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)
RENAL FAILURE [A] †	1/29 (3.45%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Respiratory, thoracic and mediastinal disorders					
RESPIRATORY DISTRESS [A] †	0/29 (0%)	0/18 (0%)	1/10 (10%)	0/9 (0%)	0/8 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.1)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Induction: ENF+HAART	Induction Phase: HAART	Maintenance Phase: ENF + HAART	Maintenance Phase: HAART (ENF Removed)	Maintenance Phase: HAART
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	9/29 (31.03%)	11/18 (61.11%)	2/10 (20%)	4/9 (44.44%)	3/8 (37.5%)
Blood and lymphatic system disorders					
THROMBOCYTOPENIA [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Ear and labyrinth disorders					

	Induction: ENF+HAART	Induction Phase: HAART	Maintenance Phase: ENF + HAART	Maintenance Phase: HAART (ENF Removed)	Maintenance Phase: HAART
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
TINNITUS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
Eye disorders					
CONJUNCTIVITIS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Gastrointestinal disorders					
ABDOMINAL DISTENSION [A] †	1/29 (3.45%)	2/18 (11.11%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
ABDOMINAL PAIN UPPER [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
CONSTIPATION [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	1/8 (12.5%)
DIARRHOEA [A] †	2/29 (6.9%)	5/18 (27.78%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
DRY MOUTH [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
DYSPHAGIA [A] †	0/29 (0%)	0/18 (0%)	1/10 (10%)	0/9 (0%)	0/8 (0%)
FLATULENCE [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
NAUSEA [A] †	1/29 (3.45%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
ODYNOPHAGIA [A] †	1/29 (3.45%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
TOOTHACHE [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
VOMITING [A] †	2/29 (6.9%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
General disorders					
CHEST PAIN [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
PAIN [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
Hepatobiliary disorders					
HEPATIC FAILURE [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Immune system disorders					
DRUG HYPERSENSITIVITY [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)

	Induction: ENF+HAART	Induction Phase: HAART	Maintenance Phase: ENF + HAART	Maintenance Phase: HAART (ENF Removed)	Maintenance Phase: HAART
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Infections and infestations					
ABSCESS JAW [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)
BRONCHITIS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
CELLULITIS [A] †	2/29 (6.9%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
FOLLICULITIS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
GINGIVAL ABSCESS [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
INFLUENZA [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
NASOPHARYNGITIS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
ONYCHOMYCOSIS [A] †	0/29 (0%)	0/18 (0%)	1/10 (10%)	0/9 (0%)	0/8 (0%)
PHARYNGITIS [A] †	0/29 (0%)	1/18 (5.56%)	1/10 (10%)	1/9 (11.11%)	1/8 (12.5%)
PNEUMONIA BACTERIAL [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)
Injury, poisoning and procedural complications					
SKIN INJURY [A] †	0/29 (0%)	0/18 (0%)	1/10 (10%)	0/9 (0%)	0/8 (0%)
Investigations					
PLATELET COUNT DECREASED [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
TRANSAMINASES INCREASED [A] †	0/29 (0%)	2/18 (11.11%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Metabolism and nutrition disorders					
ANOREXIA [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
HYPERCHOLESTEROLAEMIA [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)
HYPERTRIGLYCERIDAEMIA [A] †	0/29 (0%)	0/18 (0%)	0/10 (0%)	1/9 (11.11%)	0/8 (0%)
Musculoskeletal and connective tissue disorders					
MUSCULOSKELETAL CHEST PAIN [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)

	Induction: ENF+HAART	Induction Phase: HAART	Maintenance Phase: ENF + HAART	Maintenance Phase: HAART (ENF Removed)	Maintenance Phase: HAART
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Nervous system disorders					
DIZZINESS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
HEADACHE [A] †	1/29 (3.45%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Psychiatric disorders					
INSOMNIA [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Respiratory, thoracic and mediastinal disorders					
COUGH [A] †	1/29 (3.45%)	0/18 (0%)	1/10 (10%)	1/9 (11.11%)	1/8 (12.5%)
EPISTAXIS [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	1/8 (12.5%)
PULMONARY CONGESTION [A] †	0/29 (0%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)
Skin and subcutaneous tissue disorders					
RASH [A] †	1/29 (3.45%)	1/18 (5.56%)	0/10 (0%)	0/9 (0%)	0/8 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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