



Clinical trial results:

Biojector 2000 Open-Label Safety Study (BOSS) to Evaluate Signs and Symptoms Associated With a Needle-free Injection Device for Administration of Fuzeon to Patients With HIV-1 Infection

Summary

EudraCT number	2016-000263-17
Trial protocol	Outside EU/EEA
Global end of trial date	04 December 2006

Results information

Result version number	v1 (current)
This version publication date	09 December 2016
First version publication date	09 December 2016

Trial information

Trial identification

Sponsor protocol code	ML19849
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00337701
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 6912
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

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	04 December 2006
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 December 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To compare injection site reaction (ISR) signs and symptoms associated with enfuvirtide (ENF) injection using needle/syringe (NS) versus Biojector 2000 (B2000) needle-free injection device (NFID) based on a composite endpoint of grade 1-3 ongoing pain and either (a) grade 3-4 induration (≥ 25 mm) or (b) grade 2-4 nodules/cysts (> 20 mm).
- To compare the incidence and severity of individual clinical signs and symptoms of ISR associated with ENF injection using NS versus B2000 NFID.

Protection of trial subjects:

All study subjects were required to read and sign an informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 317
Worldwide total number of subjects	317
EEA total number of subjects	0

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)	2
Adults (18-64 years)	309
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 349 subjects were enrolled at 42 centres in the United States. Out of 349 subjects, 317 subjects received at least 1 dose of study drug and had at least 1 post-baseline safety assessment. These were included in the safety population and all analyses were performed on the safety population set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator ^[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Biojector 2000

Arm description:

Subjects self-administered enfuvirtide (ENF) using Biojector 2000 (B2000) from Day 1 through the end of the study (Day 57).

Arm type	Experimental
Investigational medicinal product name	Enfuvirtide (ENF)
Investigational medicinal product code	
Other name	Fuzeon
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Enfuvirtide (ENF) 90 milligram (mg), subcutaneously (SC) twice daily (BID).

Arm title	First Needle/Syringe Then Biojector 2000
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Arm description:

Subjects self-administered ENF using needle/syringe (NS) from Day 1 through Day 28 followed by self-administration of ENF using B2000 from Day 29 up to Day 57.

Arm type	Experimental
Investigational medicinal product name	Enfuvirtide (ENF)
Investigational medicinal product code	
Other name	Fuzeon
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Enfuvirtide (ENF) 90 mg, SC twice daily.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Injection site reaction (ISR) evaluator was blinded through Week 4.

Number of subjects in period 1	Biojector 2000	First Needle/Syringe Then Biojector 2000
Started	213	104
Completed	187	97
Not completed	26	7
Withdrew Consent	5	1
Adverse Event	3	1
Injection Site Reaction	11	2
Lost to follow-up	2	1
Reason not Specified	2	1
Difficulty With Injection Device	3	1

Baseline characteristics

Reporting groups

Reporting group title	Biojector 2000
Reporting group description: Subjects self-administered enfuvirtide (ENF) using Biojector 2000 (B2000) from Day 1 through the end of the study (Day 57).	
Reporting group title	First Needle/Syringe Then Biojector 2000
Reporting group description: Subjects self-administered ENF using needle/syringe (NS) from Day 1 through Day 28 followed by self-administration of ENF using B2000 from Day 29 up to Day 57.	

Reporting group values	Biojector 2000	First Needle/Syringe Then Biojector 2000	Total
Number of subjects	213	104	317
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	46.9	46.5	
standard deviation	± 7.6	± 7.9	-
Gender categorical Units: Subjects			
Female	21	10	31
Male	192	94	286

End points

End points reporting groups

Reporting group title	Biojector 2000
Reporting group description: Subjects self-administered enfuvirtide (ENF) using Biojector 2000 (B2000) from Day 1 through the end of the study (Day 57).	
Reporting group title	First Needle/Syringe Then Biojector 2000
Reporting group description: Subjects self-administered ENF using needle/syringe (NS) from Day 1 through Day 28 followed by self-administration of ENF using B2000 from Day 29 up to Day 57.	

Primary: Percentage of Subjects With the Composite Tolerability Endpoint (Painful Induration or Nodules/Cysts) at Baseline

End point title	Percentage of Subjects With the Composite Tolerability Endpoint (Painful Induration or Nodules/Cysts) at Baseline ^[1]
End point description: Subjects with any injection site reaction (ISR) with grade 1-3 ongoing pain and either grade 3-4 induration (greater than or equal to \geq 25 millimeters [mm]) or grade 2-4 nodules/cysts (>20 mm). Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.	
End point type	Primary
End point timeframe: Baseline (Day 1)	

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: Statistical analyses were not performed for this endpoint.

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	104		
Units: percentage of subjects				
number (not applicable)	40.1	36.5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With the Composite Tolerability Endpoint (Painful Induration or Nodules/Cysts) at Week 4

End point title	Percentage of Subjects With the Composite Tolerability Endpoint (Painful Induration or Nodules/Cysts) at Week 4
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End point description:

Subjects with any ISR with grade 1-3 ongoing pain and either grade 3-4 induration (≥ 25 mm) or grade 2-4 nodules/cysts (> 20 mm). Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Week 4

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	102		
Units: percentage of subjects				
number (not applicable)	25.4	45.1		

Statistical analyses

Statistical analysis title	Composite Tolerability Endpoint
Comparison groups	Biojector 2000 v First Needle/Syringe Then Biojector 2000
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0003 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[2] - P value was based on Cochran-Mantel-Haenszel test using randomization strata on week 4 data.

Primary: Percentage of Subjects With the Composite Tolerability Endpoint (Painful Induration or Nodules/Cysts) at Week 8

End point title	Percentage of Subjects With the Composite Tolerability Endpoint (Painful Induration or Nodules/Cysts) at Week 8 ^[3]
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End point description:

Subjects with any ISR with grade 1-3 ongoing pain and either grade 3-4 induration (≥ 25 mm) or grade 2-4 nodules/cysts (> 20 mm). Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Week 8

Notes:

[3] - 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: Statistical analyses were not performed for this endpoint.

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	92		
Units: percentage of subjects				
number (not applicable)	21.2	26.1		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Injection Site Reactions by Sign/Symptom and Grade at Baseline

End point title	Percentage of Subjects with Injection Site Reactions by Sign/Symptom and Grade at Baseline ^[4]
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End point description:

Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Baseline

Notes:

[4] - 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: Statistical analyses were not performed for this endpoint.

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	104		
Units: percentage of subjects				
number (not applicable)				
Any ISR: Grade 1	80.2	76.9		
Any ISR: Grade 2	72.2	69.2		
Any ISR: Grade 3	54.2	57.7		
Any ISR: Grade 4	26.4	26		
Any ISR: Any Grade	88.7	86.5		
Ongoing Pain/Discomfort: Grade 1	53.8	46.2		
Ongoing Pain/Discomfort: Grade 2	24.5	27.9		
Ongoing Pain/Discomfort: Grade 3	1.4	5.8		
Ongoing Pain/Discomfort: Any Grade	64.2	56.7		
Erythema: Grade 1	31.6	37.5		
Erythema: Grade 2	32.1	29.8		
Erythema: Grade 3	21.7	14.4		
Erythema: Grade 4	2.8	3.8		
Erythema: Any Grade	57.5	58.7		

Induration: Grade 1	22.2	28.8		
Induration: Grade 2	38.7	40.4		
Induration: Grade 3	44.3	43.3		
Induration: Grade 4	25.5	25		
Induration: Any Grade	71.2	75		
Pruritus: Grade 1	19.3	17.3		
Pruritus: Grade 2	0.9	0		
Pruritus: Any Grade	19.3	17.3		
Nodules/Cysts: Grade 1	36.8	31.7		
Nodules/Cysts: Grade 2	29.7	26		
Nodules/Cysts: Grade 3	18.9	17.3		
Nodules/Cysts: Grade 4	1.4	0		
Nodules/Cysts: Any Grade	54.2	47.1		
Ecchymosis: Grade 1	15.1	20.2		
Ecchymosis: Grade 2	6.1	7.7		
Ecchymosis: Grade 3	3.8	5.8		
Ecchymosis: Grade 4	1.9	1		
Ecchymosis: Any Grade	24.5	27.9		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Injection Site Reactions by Sign/Symptom and Grade at Week 4

End point title	Percentage of Subjects with Injection Site Reactions by Sign/Symptom and Grade at Week 4 ^[5]
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End point description:

Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Week 4

Notes:

[5] - 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: Statistical analyses were not performed for this endpoint.

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	102		
Units: percentage of subjects				
number (not applicable)				
Any ISR: Grade 1	74.1	79.4		
Any ISR: Grade 2	64.4	74.5		
Any ISR: Grade 3	46.8	60.8		

Any ISR: Grade 4	22.9	23.5		
Any ISR: Any Grade	85.9	95.1		
Ongoing Pain/Discomfort: Grade 1	40.5	56.9		
Ongoing Pain/Discomfort: Grade 2	16.1	28.4		
Ongoing Pain/Discomfort: Grade 3	2.4	4.9		
Ongoing Pain/Discomfort: Any Grade	47.3	67.6		
Erythema: Grade 1	34.1	33.3		
Erythema: Grade 2	21.5	31.4		
Erythema: Grade 3	11.7	22.5		
Erythema: Grade 4	4.4	2.9		
Erythema: Any Grade	49.8	61.8		
Induration: Grade 1	20.5	28.4		
Induration: Grade 2	37.6	38.2		
Induration: Grade 3	36.1	48		
Induration: Grade 4	19.5	20.6		
Induration: Any Grade	65.4	75.5		
Pruritus: Grade 1	7.8	16.7		
Pruritus: Grade 2	1	1		
Pruritus: Any Grade	8.3	17.6		
Nodules/Cysts: Grade 1	31.7	29.4		
Nodules/Cysts: Grade 2	19.5	29.4		
Nodules/Cysts: Grade 3	16.6	18.6		
Nodules/Cysts: Grade 4	0	0		
Nodules/Cysts: Any Grade	42.9	48		
Ecchymosis: Grade 1	22	17.6		
Ecchymosis: Grade 2	8.3	10.8		
Ecchymosis: Grade 3	6.8	2		
Ecchymosis: Grade 4	3.9	2.9		
Ecchymosis: Any Grade	28.8	26.5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Injection Site Reactions by Sign/Symptom and Grade at Week 8

End point title	Percentage of Subjects with Injection Site Reactions by Sign/Symptom and Grade at Week 8 ^[6]
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End point description:

Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Week 8

Notes:

[6] - 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: Statistical analyses were not performed for this endpoint.

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	92		
Units: percentage of subjects				
number (not applicable)				
Any ISR: Grade 1	67.9	72.8		
Any ISR: Grade 2	54.3	55.4		
Any ISR: Grade 3	44.6	45.7		
Any ISR: Grade 4	20.7	19.6		
Any ISR: Any Grade	79.9	84.8		
Ongoing Pain/Discomfort: Grade 1	32.6	50		
Ongoing Pain/Discomfort: Grade 2	14.1	12		
Ongoing Pain/Discomfort: Grade 3	1.6	2.2		
Ongoing Pain/Discomfort: Any Grade	37.5	54.3		
Erythema: Grade 1	31.5	30.4		
Erythema: Grade 2	22.3	21.7		
Erythema: Grade 3	11.4	5.4		
Erythema: Grade 4	3.8	2.2		
Erythema: Any Grade	48.4	46.7		
Induration: Grade 1	22.3	18.5		
Induration: Grade 2	30.4	32.6		
Induration: Grade 3	38.6	35.9		
Induration: Grade 4	17.4	18.5		
Induration: Any Grade	65.8	65.2		
Pruritus: Grade 1	8.7	9.8		
Pruritus: Grade 2	0.5	0		
Pruritus: Any Grade	8.7	9.8		
Nodules/Cysts: Grade 1	28.8	23.9		
Nodules/Cysts: Grade 2	17.4	13		
Nodules/Cysts: Grade 3	10.9	7.6		
Nodules/Cysts: Grade 4	0	0		
Nodules/Cysts: Any Grade	33.7	31.5		
Ecchymosis: Grade 1	27.7	25		
Ecchymosis: Grade 2	8.2	9.8		
Ecchymosis: Grade 3	3.8	4.3		
Ecchymosis: Grade 4	3.3	2.2		
Ecchymosis: Any Grade	32.6	32.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Injection Site Reaction Score at Baseline and Week 4 – Between-Subject Comparison

End point title	Overall Injection Site Reaction Score at Baseline and Week 4 – Between- Subject Comparison
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End point description:

Injection site reaction (ISR) score is calculated for each individual sign/symptom as $\sum g_i n_i$, where $i = 1$ to the total number of ISRs, g = grade (ie, 1-3 for ongoing pain and pruritus and 1-4 for all others), and n = frequency. The individual scores were summed to give an overall total ISR score for each visit. The maximum possible overall score for a single ISR is 22. Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint and 'n'=number of subjects who were evaluated at specific time points.

End point type	Secondary
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End point timeframe:

Baseline and Week 4

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	104		
Units: unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n=212, 104)	20.2 (± 19.8)	19.7 (± 18.8)		
Week 4 (n=205, 102)	15.3 (± 15.99)	19.2 (± 14.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Injection Site Reaction Score at Baseline and Post-baseline in the Needle/Syringe to Biojector 2000 Group – Within-Subject Comparison

End point title	Overall Injection Site Reaction Score at Baseline and Post-baseline in the Needle/Syringe to Biojector 2000 Group – Within-Subject Comparison
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End point description:

Injection site reaction (ISR) score is calculated for each individual sign/symptom as $\sum g_i n_i$, where $i = 1$ to the total number of ISRs, g = grade (ie, 1-3 for ongoing pain and pruritus and 1-4 for all others), and n = frequency. The individual scores were summed to give an overall total ISR score for each visit. The maximum possible overall score for a single ISR is 22. Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint and 'n'=number of subjects who were evaluated at specific time points.

End point type	Secondary
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End point timeframe:

Baseline and Week 4

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	91		
Units: unit on a scale				
arithmetic mean (standard deviation)				
Baseline	19 (± 18.06)	19 (± 18.06)		
Week 4 (Needle/Syringe)/Week 8 (Biojector 2000)	19 (± 14.21)	11.4 (± 10.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Discontinuing with Injection Site Reactions Leading to Discontinuation

End point title	Percentage of Subjects Discontinuing with Injection Site Reactions Leading to Discontinuation
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End point description:

Injection site reactions leading to discontinuation were tabulated and listed by device used at the time of discontinuation. Safety analysis set included all subjects who received at least 1 dose of study medication and completed at least 1 post-baseline safety assessment on the randomized device. A post-baseline assessment is defined as any clinical evaluation for adverse events, local injection site reactions or death reported after the first dose of study medication. Here, number of subjects analysed is the total number of subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline up to 8 weeks

End point values	Biojector 2000	First Needle/Syringe Then Biojector 2000		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	104		
Units: percentage of subjects				
number (not applicable)	6.1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Baseline up to Week 8

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.0
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Reporting groups

Reporting group title	Biojector 2000
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Reporting group description:

Subjects self-administered enfuvirtide (ENF) using Biojector 2000 (B2000) from Day 1 through the end of the study (Day 57).

Reporting group title	First Needle/Syringe Then Biojector 2000
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Reporting group description:

Subjects self-administered ENF using needle/syringe (NS) from Day 1 through Day 28 followed by self-administration of ENF using B2000 from Day 29 up to Day 57.

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: Only selected safety data were collected, which included serious adverse events (SAEs), serious AIDS-defining events, discontinuations (of ENF and/or the injection device), adverse events of special interest, and AEs needed to clarify SAEs or discontinuations. Hence, non-serious adverse events were not collected.

Serious adverse events	Biojector 2000	First Needle/Syringe Then Biojector 2000	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 213 (2.82%)	4 / 104 (3.85%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 213 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 213 (0.00%)	2 / 104 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			
subjects affected / exposed	0 / 213 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 213 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (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			
Streptococcal sepsis			
subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 213 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 213 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 213 (0.47%)	0 / 104 (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: 0 %

Non-serious adverse events	Biojector 2000	First Needle/Syringe Then Biojector 2000	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 213 (0.00%)	0 / 104 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2006	1. The protocol was amended primarily to capture all adverse events (AEs) that may be related to injection devices. These AEs are referred to as 'adverse events of special interest' and are defined as any device-related (B2000 or needle/syringe) AE other than the expected signs or symptoms of localized ISRs. 2. The amended protocol provided examples of the types of AEs to be reported, and investigators were asked to only record adverse events that could be considered related to the injection device.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported