# 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 |

**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 |

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 [≥] 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 |

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 |

End point description:

Injection site reaction (ISR) score is calculated for each individual sign/symptom as Σgini, 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 |
|---|---|

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 |
|---|---|

End point description:

Injection site reaction (ISR) score is calculated for each individual sign/symptom as Σgini, 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 9.0 |

### 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.

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.<br>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