



Clinical trial results:

A multicentre, double blind, randomized placebo controlled trial to assess the effect of LF-PB on seroma formation in women with breast cancer undergoing Axillary Lymph Node Dissection

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-005289-31 |
| Trial protocol | IT |
| Global end of trial date | 19 July 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 24 May 2020 |
| First version publication date | 24 May 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | LF-PB/14/05 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02668588 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | ND: ND |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Chemi S.p.A. |
| Sponsor organisation address | Via dei Laboratori 54, Cinisello Balsamo, MI, Italy, 20092 |
| Public contact | Clinical Research and Development Director, Chemi S.p.A, +39 02 6443 1, p.bettica@italfarmaco.com |
| Scientific contact | Clinical Research and Development Director, Chemi S.p.A, +39 02 64431, p.bettica@italfarmaco.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 | 19 July 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 July 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 July 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives were:

- To assess the effect of LF-PB 30 mg versus placebo on seroma incidence by Day 28 after ALND.
- To assess the safety and tolerability of LF-PB 30 mg.

Protection of trial subjects:

The trial was conducted in accordance with the Helsinki Declaration and the International Council for Harmonisation (ICH) guidelines on Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 22 October 2015 |
| 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 | Italy: 48 |
| Worldwide total number of subjects | 48 |
| EEA total number of subjects | 48 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 32 |
| From 65 to 84 years | 16 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who signed the informed consent to participate in this trial underwent screening assessments within 3 weeks from Day 0 (randomization/the day of surgery).

Period 1

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

Blinding implementation details:

This was a double-blind study. No further details on the blinding implementation are reported in the CSR/protocol of the study.

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | LF-PB 30 mg |

Arm description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | LF-PB |
| Investigational medicinal product code | |
| Other name | octreotide acetate |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular and intravenous use |

Dosage and administration details:

Subjects were dosed once with 30 mg LF-PB administered via gluteus bolus injection. Formulation: Reconstituted active product for i.m. administration. LF-PB 30 mg was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| | |
|--|-----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular and intravenous use |

Dosage and administration details:

Subjects were dosed once with placebo for LF-PB 30 mg: administered via gluteus bolus injection. Formulation: reconstituted placebo product for i.m. administration. Placebo for LF-PB 30 mg was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-

cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| Number of subjects in period 1 | LF-PB 30 mg | Placebo |
|---------------------------------------|-------------|---------|
| Started | 24 | 24 |
| Completed | 22 | 24 |
| Not completed | 2 | 0 |
| Consent withdrawn by subject | 2 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | LF-PB 30 mg |
|-----------------------|-------------|

Reporting group description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| Reporting group values | LF-PB 30 mg | Placebo | Total |
|--|-------------|---------|-------|
| Number of subjects | 24 | 24 | 48 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 16 | 17 | 33 |
| From 65-84 years | 8 | 7 | 15 |
| Gender categorical | | | |
| In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled. | | | |
| Units: Subjects | | | |
| Female | 24 | 24 | 48 |

Subject analysis sets

| | |
|----------------------------|------------------------------|
| Subject analysis set title | LF-PB 30 mg - ITT population |
|----------------------------|------------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained.

| | |
|----------------------------|--------------------------|
| Subject analysis set title | Placebo - ITT population |
|----------------------------|--------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained.

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | LF-PB 30 mg - safety population |
|----------------------------|---------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used to summarize the safety assessments.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Placebo - safety population |
|----------------------------|-----------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used

to summarize the safety assessments.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | LF-PB 30 mg - PK population |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

PK population: The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic

| | |
|----------------------------|-------------------------|
| Subject analysis set title | placebo - PK population |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | LF-PB 30 mg - PP population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | placebo - PP population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

| Reporting group values | LF-PB 30 mg - ITT population | Placebo - ITT population | LF-PB 30 mg - safety population |
|--|------------------------------|--------------------------|---------------------------------|
| Number of subjects | 24 | 24 | 24 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 16 | 17 | 16 |
| From 65-84 years | 8 | 7 | 8 |
| Gender categorical | | | |
| In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled. | | | |
| Units: Subjects | | | |
| Female | 24 | 24 | 24 |

| Reporting group values | Placebo - safety population | LF-PB 30 mg - PK population | placebo - PK population |
|--|-----------------------------|-----------------------------|-------------------------|
| Number of subjects | 24 | 24 | 24 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 17 | 16 | 17 |
| From 65-84 years | 7 | 8 | 7 |
| Gender categorical | | | |
| In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled. | | | |
| Units: Subjects | | | |
| Female | 24 | 24 | 24 |

| Reporting group values | LF-PB 30 mg - PP population | placebo - PP population | |
|--|--------------------------------|----------------------------|--|
| Number of subjects | 23 | 23 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) From 65-84 years | | | |
| Gender categorical | | | |
| In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled. | | | |
| Units: Subjects | | | |
| Female | | | |

End points

End points reporting groups

| | |
|--|---------------------------------|
| Reporting group title | LF-PB 30 mg |
| Reporting group description: LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v). | |
| Reporting group title | Placebo |
| Reporting group description: Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v). | |
| Subject analysis set title | LF-PB 30 mg - ITT population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained. | |
| Subject analysis set title | Placebo - ITT population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained. | |
| Subject analysis set title | LF-PB 30 mg - safety population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used to summarize the safety assessments. | |
| Subject analysis set title | Placebo - safety population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used to summarize the safety assessments. | |
| Subject analysis set title | LF-PB 30 mg - PK population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: PK population: The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic | |
| Subject analysis set title | placebo - PK population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic | |
| Subject analysis set title | LF-PB 30 mg - PP population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | placebo - PP population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

Primary: Incidence of seromas requiring an aspiration by day 28 on ITT population

| | |
|-----------------|--|
| End point title | Incidence of seromas requiring an aspiration by day 28 on ITT population |
|-----------------|--|

End point description:

Incidence of seromas requiring aspiration by Day 28 was calculated as the percentage of subjects who underwent an aspiration of seromas (based on the investigator's evaluation of the echography at the operated axilla) between discharge or Visit 2 (Day 3) after surgery, and Visit 7 (Day 28). In case of two or more consecutive missing visits the worst-case scenario was assumed.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

by Day 28

| End point values | LF-PB 30 mg - ITT population | Placebo - ITT population | | |
|-----------------------------|------------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 24 | 24 | | |
| Units: percentage | | | | |
| number (not applicable) | | | | |
| yes | 75.0 | 62.5 | | |
| no | 25.0 | 37.5 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | LF-PB 30 mg vs placebo |
| Comparison groups | LF-PB 30 mg - ITT population v Placebo - ITT population |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.894 ^[1] |
| Method | Fisher exact |
| Parameter estimate | difference in incidence |
| Point estimate | 12.5 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 38.5 |

Notes:

[1] - One-sided Fisher's exact test P-value

Primary: Incidence of seromas requiring an aspiration by day 28 on PP population

| | |
|-----------------|---|
| End point title | Incidence of seromas requiring an aspiration by day 28 on PP population |
|-----------------|---|

End point description:

Incidence of seromas requiring aspiration by Day 28 was calculated as the percentage of subjects who underwent an aspiration of seromas (based on the investigator's evaluation of the echography at the operated axilla) between discharge or Visit 2 (Day 3) after surgery, and Visit 7 (Day 28). In case of two or more consecutive missing visits the worst-case scenario was assumed.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

By day 28

| End point values | LF-PB 30 mg - PP population | placebo - PP population | | |
|-----------------------------|-----------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: percentage | | | | |
| number (not applicable) | | | | |
| yes | 78.3 | 65.2 | | |
| no | 21.7 | 34.8 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | LF-PB 30 mg vs placebo |
| Comparison groups | LF-PB 30 mg - PP population v placebo - PP population |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.905 |
| Method | Fisher exact |
| Parameter estimate | difference in incidence |
| Point estimate | 13 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 38.8 |

Secondary: Time to resolution of seroma

| | |
|-----------------|------------------------------|
| End point title | Time to resolution of seroma |
|-----------------|------------------------------|

End point description:

Seroma duration: seroma was considered resolved when at the corresponding visits no aspiration, based on the Investigator clinical evaluation, was required (the information was confirmed at the next visit or

at 7 days post ALND, whichever occurred first). If seroma was still present at the end of trial visit, the subject was censored. In case of recurrence of seroma (i.e. recurrence of seroma after the termination of previous one), the final duration was considered the cessation of last episode.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At days 1, 3, 7, 11, 14, 21, 28, 56, 84 | |

| End point values | LF-PB 30 mg - ITT population | Placebo - ITT population | | |
|----------------------------------|------------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 18 | 15 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 15.00 (3.0 to 23.0) | 12.00 (3.00 to 19.00) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | LF-PB 30 mg vs placebo |
| Comparison groups | LF-PB 30 mg - ITT population v Placebo - ITT population |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| P-value | = 0.534 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 2.79 |

Notes:

[2] - Hazard ratio, Confidence Interval and Likelihood Ratio test p-value are derived from Cox-proportional hazards regression model with Treatment as covariate variable

Secondary: Number of aspirations required

| | |
|---|--------------------------------|
| End point title | Number of aspirations required |
| End point description: | |
| Number of aspirations when volume aspirate was more than zero. In case of recurrent seroma, the number of aspirations was cumulative. | |
| End point type | Secondary |
| End point timeframe: | |
| At days 3, 7, 11, 14, 21, 28, 56, 84 | |

| End point values | LF-PB 30 mg - ITT population | Placebo - ITT population | | |
|--------------------------------------|------------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 18 | 15 | | |
| Units: number | | | | |
| arithmetic mean (standard deviation) | 3.6 (± 2.50) | 4.1 (± 3.33) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | LF-PB 30 mg vs placebo |
| Comparison groups | LF-PB 30 mg - ITT population v Placebo - ITT population |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.884 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Total volume of fluid aspirated from seroma

| | |
|------------------------|---|
| End point title | Total volume of fluid aspirated from seroma |
| End point description: | Total Volume of Fluid aspirated from seroma after drain removal |
| End point type | Secondary |
| End point timeframe: | At days 1, 3, 7, 11, 14, 21, 28, 56, 84 |

| End point values | LF-PB 30 mg - ITT population | Placebo - ITT population | | |
|--------------------------------------|------------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 18 | 15 | | |
| Units: mL | | | | |
| arithmetic mean (standard deviation) | 461.1 (± 654.96) | 445.0 (± 554.13) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax

| | |
|------------------------|---|
| End point title | Cmax |
| End point description: | PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4) |
| End point type | Secondary |

End point timeframe:

Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28.

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | LF-PB 30 mg - PK population | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 24 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 16.35 (± 8.24) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax

| | |
|---|-----------|
| End point title | Tmax |
| End point description: PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4) | |
| End point type | Secondary |
| End point timeframe: Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28. | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | LF-PB 30 mg - PK population | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 24 | | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 21.17 (± 25.28) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUClast

| | |
|---|-----------|
| End point title | AUClast |
| End point description: PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4) | |
| End point type | Secondary |
| End point timeframe: Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28. | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | LF-PB 30 mg - PK population | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 24 | | | |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | 2229.28 (± 822.39) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: T1/2,z

| | |
|---|-----------|
| End point title | T1/2,z |
| End point description: | |
| PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4) | |
| End point type | Secondary |
| End point timeframe: | |
| Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28. | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | LF-PB 30 mg - PK population | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 97.86 (± 64.23) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study, AE data will be obtained at all study visits, based on information spontaneously provided by the patient and/or through questioning

Adverse event reporting additional description:

An Adverse Event is "any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment". (ICH E2A)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | LF-PB 30 mg |
|-----------------------|-------------|

Reporting group description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

| Serious adverse events | LF-PB 30 mg | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 1 / 24 (4.17%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 1 / 24 (4.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | LF-PB 30 mg | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 24 (58.33%) | 14 / 24 (58.33%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm recurrence | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 24 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Dry gangrene | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 24 (4.17%) | |
| occurrences (all) | 0 | 1 | |
| Hot flush | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 24 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 24 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 24 (4.17%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | 4 / 24 (16.67%) | |
| occurrences (all) | 4 | 7 | |
| Injection site pain | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 2 / 24 (8.33%) | |
| occurrences (all) | 3 | 2 | |
| Pain | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 1 / 24 (4.17%) | |
| occurrences (all) | 3 | 1 | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 2 / 24 (8.33%) | |
| occurrences (all) | 0 | 2 | |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 24 (4.17%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|--|--|
| Injection site urticaria subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 24 (0.00%) 0 | |
| Reproductive system and breast disorders Breast inflammation subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 24 (4.17%) 1 | |
| Investigations Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 24 (0.00%) 0 | |
| Injury, poisoning and procedural complications Anaemia postoperative subjects affected / exposed occurrences (all) Eschar subjects affected / exposed occurrences (all) Wound complication subjects affected / exposed occurrences (all) Wound dehiscence subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 0 / 24 (0.00%) 0 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | 0 / 24 (0.00%) 0 1 / 24 (4.17%) 1 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 | |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 24 (0.00%) 0 | |
| Nervous system disorders Syncope subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 24 (4.17%) 1 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 1 / 24 (4.17%) 1 | |

| | | | |
|--|--|--|--|
| Leukopenia subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 24 (0.00%) 0 | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 24 (4.17%) 1 | |
| Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 5 / 24 (20.83%) 5 3 / 24 (12.50%) 3 2 / 24 (8.33%) 2 | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 2 / 24 (8.33%) 2 | |
| Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash erythematous subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 0 / 24 (0.00%) 0 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 2 / 24 (8.33%) 2 | |
| Infections and infestations | | | |

| | | | |
|---|---------------------|---------------------|--|
| Wound infection subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | 0 / 24 (0.00%) 0 | |
|---|---------------------|---------------------|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| No limitations or caveats are applicable to this summary of the results |
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Notes: