



Clinical trial results:

Comparative Study, intraindividual to evaluate efficacy and safety of the treatment of actinic keratosis with photodynamic therapy between methyl aminolevulinate cream and aminolevulinic acid nanosome gel

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-002408-97 |
| Trial protocol | ES |
| Global end of trial date | 21 June 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 28 June 2021 |
| First version publication date | 28 June 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | MALvsALA |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02647151 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Carlos Serra - Fundación Instituto Valenciano de Oncología |
| Sponsor organisation address | C/. Profesor Beltrán Baguena, n.º 8 , Valencia, Spain, 46009 |
| Public contact | Federico Nepote, Marketing Farmacéutico & Investigación Clínica, 0034 934344412, investigacion@mfar.net |
| Scientific contact | Federico Nepote, Marketing Farmacéutico & Investigación Clínica, 0034 934344412, investigacion@mfar.net |

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 | 21 February 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 June 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 June 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare MAL with the new photosensitizer BF-200 ALA in terms of local reaction and tolerability of the QA treatment

Protection of trial subjects:

All procedures were performed in accordance to Good clinical practice guidelines, the ICH principles for development of clinical research derived from the declaration of Helsinki and its later update fortaleza 2013. This clinical trial was approved by the local competent authorities in Spain and was developed in compliance to the current local regulations in terms of clinical research and data protection. The protocol already includes measures to mitigate risk and protection of subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 03 August 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 | Spain: 22 |
| Worldwide total number of subjects | 22 |
| EEA total number of subjects | 22 |

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) | 12 |
| From 65 to 84 years | 10 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In order to achieve masking of the treatment by the researchers, the initial visit where the patient's data was collected and the treatment area was randomly assigned to each of the photosensitizers, was carried out by a different dermatologist from the one who evaluated the variables of the study

Period 1

| | |
|------------------------------|-------------------------------------|
| Period 1 title | Whole study period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

In order to achieve masking of the treatment by the researchers, the initial visit where the patient's data was collected and the treatment area was randomly assigned to each of the photosensitizers, was carried out by a different dermatologist from the one who evaluated the variables of the study

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | No |
| Arm title | BF-200 ALA |

Arm description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.

The patients were administered with BF-200 ALA in the allocated region.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BF-200 ALA |
| Investigational medicinal product code | ATC: L01XD04 |
| Other name | Ameluz 78 mg/g gel |
| Pharmaceutical forms | Gel |
| Routes of administration | Topical use |

Dosage and administration details:

1 application previous to phototherapy. 78 mg/g

| | |
|------------------|-----------|
| Arm title | MAL cream |
|------------------|-----------|

Arm description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.

The patients were administered with MAL in the allocated region.

| | |
|--|-----------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | MAL |
| Investigational medicinal product code | ATC: L01X D03 |
| Other name | Metvix 160 mg/g cream |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:

1 dose administration. 160 mg/g

| Number of subjects in period 1 | BF-200 ALA | MAL cream |
|---------------------------------------|------------|-----------|
| Started | 22 | 22 |
| Completed | 22 | 22 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Whole study period |
|-----------------------|--------------------|

Reporting group description: -

| Reporting group values | Whole study period | Total | |
|--|--------------------|-------|--|
| Number of subjects | 22 | 22 | |
| 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 | | | |
| Patient age at inclusion | | | |
| Units: years | | | |
| log mean | 72 | | |
| full range (min-max) | 57 to 84 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | 1 | |
| Male | 21 | 21 | |
| Treatment region | | | |
| Body region where the patient was treated. Each patient received both treatments in simetric and similar body regions | | | |
| Units: Subjects | | | |
| scalp | 12 | 12 | |
| forehead | 6 | 6 | |
| cheek | 4 | 4 | |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | BF-200 ALA |
| Reporting group description: Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions. The patients were administered with BF-200 ALA in the allocated region. | |
| Reporting group title | MAL cream |
| Reporting group description: Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions. The patients were administered with MAL in the allocated region. | |

Primary: Immediate local reaction

| | |
|--|--------------------------|
| End point title | Immediate local reaction |
| End point description: The immediate local reaction to illumination may include, to a greater or lesser degree, erythema, inflammation, and edema. It will be scored on a scale from 0 to 10 where 0 will be normal skin, without local reaction and 10 a maximum local reaction. | |
| End point type | Primary |
| End point timeframe: First visit, treatment administration | |

| End point values | BF-200 ALA | MAL cream | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: Arbitrary unit | | | | |
| arithmetic mean (standard deviation) | 5.4 (\pm 1.96) | 4.7 (\pm 1.96) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | ANOVA 1 factor |
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.255 |
| Method | ANOVA |

Primary: Late local reaction

| | |
|-----------------|---------------------|
| End point title | Late local reaction |
|-----------------|---------------------|

End point description:

The late local reaction defined by the presence to a greater or lesser degree of erythema, inflammation, edema, scabs and pustules, will also be scored from 0 to 10 where 0 will be normal skin, no local reaction and 10 a maximum local reaction.

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

End point timeframe:

Second visit (day 2-3 after treatment administration)

| End point values | BF-200 ALA | MAL cream | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: Arbitrary unit | | | | |
| arithmetic mean (standard deviation) | 7.4 (\pm 1.92) | 5.9 (\pm 1.92) | | |

Statistical analyses

| Statistical analysis title | ANOVA 1 factor |
|---|------------------------|
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.049 |
| Method | ANOVA |

Primary: Pain

| | |
|-----------------|------|
| End point title | Pain |
|-----------------|------|

End point description:

Pain experienced by patients is measured using a subjective, 10-cm visual analog scale. The most frequent symptoms are pain and burning sensations on the skin, beginning during lighting or shortly after, and lasting a few hours, usually resolving on the day of treatment. The severity is normally mild to moderate, and rarely, requires a premature interruption of lighting.

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

End point timeframe:

First visit, treatment administration

| End point values | BF-200 ALA | MAL cream | | |
|--------------------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: Arbitrary unit | | | | |
| arithmetic mean (standard deviation) | 5.2 (\pm 2.6) | 5 (\pm 2.6) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | ANOVA 1 factor |
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.956 |
| Method | ANOVA |

Secondary: Qeratosis lesion number on each patient

| | |
|------------------------|---|
| End point title | Qeratosis lesion number on each patient |
| End point description: | extension of the treated lesions |
| End point type | Secondary |
| End point timeframe: | Baseline |

| | | | | |
|--------------------------------------|-----------------|-----------------|--|--|
| End point values | BF-200 ALA | MAL cream | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: number of lesions | | | | |
| arithmetic mean (standard deviation) | 13.4 (± 4.4) | 14.7 (± 4.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fluorescence emission

| | |
|------------------------|--|
| End point title | Fluorescence emission |
| End point description: | Fluorescence will be studied with a Wood light lamp immediately before illumination and this can be scored from 0 to 10, where 0 was an absolute absence of fluorescence, 5 a limited and selective fluorescence in the QA lesions and 10 a fluorescence in the entire treatment area where the photosensitizer had been applied . |
| End point type | Secondary |
| End point timeframe: | |
| Selection visit | |

| End point values | BF-200 ALA | MAL cream | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: Arbitrary unit | | | | |
| arithmetic mean (standard deviation) | 6.9 (\pm 2.01) | 5.3 (\pm 2.01) | | |

Statistical analyses

| Statistical analysis title | 1 factor ANOVA |
|--|------------------------|
| Statistical analysis description: | |
| Descriptive comparison between two means and SD. | |
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.026 |
| Method | ANOVA |

Secondary: Treatment satisfaction

| End point title | Treatment satisfaction |
|--|------------------------|
| End point description: | |
| The patients will be asked about the satisfaction provided by the treatment in each of the areas (benefit obtained in relation to the discomfort and discomfort of the treatment) to obtain an answer in the form of a score from 0 to 10 where 0 is absolutely dissatisfied and 10 Totally satisfied. | |
| End point type | Secondary |
| End point timeframe: | |
| Visit 3, 30 days after treatment administration | |

| End point values | BF-200 ALA | MAL cream | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: Arbitrary unit | | | | |
| arithmetic mean (standard deviation) | 7.5 (\pm 3.8) | 7.4 (\pm 3.8) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | ANOVA 1 factor |
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.938 |
| Method | ANOVA |

Secondary: Percentage of resolved Qeratosis lesions (QAs)

| | |
|------------------------|---|
| End point title | Percentage of resolved Qeratosis lesions (QAs) |
| End point description: | Percentage of queratosis lesions resolved. |
| End point type | Secondary |
| End point timeframe: | visit 3, 30 days after treatment administration |

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | BF-200 ALA | MAL cream | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: Number of lesions | | | | |
| Resolved | 84 | 81 | | |
| Not resolved | 16 | 19 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | ANOVA 1 factor |
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.7012 |
| Method | ANOVA |

Secondary: Clinical response to treatment

| | |
|------------------------|---|
| End point title | Clinical response to treatment |
| End point description: | The clinical response will be assessed with the help of the initial photograph and the transparent template. Partial response (PR) is defined if $\geq 75\%$ of the initial AKs are resolved and complete response (CR) if 100% of them are resolved. |
| End point type | Secondary |

End point timeframe:

Visit 3, 30 days after treatment administration

| End point values | BF-200 ALA | MAL cream | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 22 | | |
| Units: patients | | | | |
| Complete response | 13 | 11 | | |
| Partial response | 5 | 7 | | |
| No response | 4 | 4 | | |

Statistical analyses

| Statistical analysis title | Complete response comparison between arms |
|--|---|
| Statistical analysis description: The percentage of patients with complete response was compared between treatment arms | |
| Comparison groups | MAL cream v BF-200 ALA |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.5448 |
| Method | ANOVA |

| Statistical analysis title | Partial response comparison between arms |
|---|--|
| Statistical analysis description: The percentage of patients with partial response among treatment arms was compared | |
| Comparison groups | BF-200 ALA v MAL cream |
| Number of subjects included in analysis | 44 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.735 |
| Method | ANOVA |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

The sponsor collected adverse events (AEs) up to 30 days after administration of the last dose of study treatment.

Adverse event reporting additional description:

Patients experienced no adverse events during the 30 days of participation in this trial.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 23 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | BF-200 ALA |
|-----------------------|------------|

Reporting group description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.

The patients were administered with BF-200 ALA in the allocated region.

| | |
|-----------------------|-----------|
| Reporting group title | MAL cream |
|-----------------------|-----------|

Reporting group description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.

The patients were administered with MAL in the allocated region.

| Serious adverse events | BF-200 ALA | MAL cream | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 22 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

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

| Non-serious adverse events | BF-200 ALA | MAL cream | |
|---|----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 0 / 22 (0.00%) | |

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: We confirm there were no Adverse events reported throughout the trial. This is consistent with the type of treatment, the pathology and the study design

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

None reported