# Clinical trial results:
# Advances in the management of mandibular osteoradionecrosis: Pentoxyfilline and Tocopherol as medical treatment.

## Summary

| | |
|---|---|
| EudraCT number | 2014-004975-22 |
| Trial protocol | ES |
| Global end of trial date | 31 January 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 September 2021 |
| First version publication date | 19 September 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | ORN-2014-16 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | VHIR |
| Sponsor organisation address | Passeig Vall Hebron 119-129, Barcelona, Spain, 08035 |
| Public contact | Joaquin Lopez-Soriano, VHIR, 34 934894779, joaquin.lopez.soriano@vhir.org |
| Scientific contact | Maxillofacial Department, Oral and Maxillofacial Surgery Department of Vall d'Hebron Hospital, 34 620684875, miryam-martos@hotmail.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 | 31 January 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 31 January 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Healing of mandibular osteoradionecrosis in patients irradiated for head and neck cance after treatment with Pentoxifilina and Tocopherol (PENTO)

Protection of trial subjects:

A mandibular TC was done if any suspects of clinical deterioration were detected. Antibiotic tretament was started in case of confirmation of an infection after microbiologal examination of exudates

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 08 March 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: 25 |
| Worldwide total number of subjects | 25 |
| EEA total number of subjects | 25 |

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) | 25 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 25 |
| Number of subjects completed | 25 |

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

After signing consent, a simple randomization was done, by giving a letter to the patient where the tretament groups was especified. Patient and clinicians knew at every moment the group to which the patient was assigned

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | PTX Tocopherol |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Pentoxifylline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Oral ingesta of 800 mg pentoxifylline (2x 400 mg tablets), daily, between 6 and 18 months

| | |
|---|---|
| Investigational medicinal product name | Tocopherol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1000 UI tocopherol (2x 400UI tablets +1x 200)UI tablet), daily, between 6 and 18 months

| | |
|---|---|
| **Arm title** | Control no treatment |

Arm description: -

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| **Number of subjects in period 1** | PTX Tocopherol | Control no treatment |
|---|---|---|
| Started | 13 | 12 |
| Completed | 13 | 12 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall trial |

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 25 | 25 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 14 | 14 | |
| From 65-84 years | 11 | 11 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 5 | 5 | |
| Male | 20 | 20 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | PTX Tocopherol |
| Reporting group description: - | |
| Reporting group title | Control no treatment |
| Reporting group description: - | |

### Primary: Intraoral ulceration reduction

| | |
|---|---|
| End point title | Intraoral ulceration reduction |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| 18 months | |

| End point values | PTX Tocopherol | Control no treatment | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 12 | | |
| Units: square millimiter | | | | |
| median (full range (min-max)) | -100 (-108 to -50) | -2 (-21 to 0) | | |

### Statistical analyses

| Statistical analysis title | Bone exposition |
|---|---|
| Comparison groups | PTX Tocopherol v Control no treatment |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |

### Secondary: Oral aperture

| | |
|---|---|
| End point title | Oral aperture |
| End point description: | |
| End point type | Secondary |

End point timeframe:
3 months

| **End point values** | PTX Tocopherol | Control no treatment | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 12 | | |
| Units: millimeter(s) | | | | |
| median (full range (min-max)) | 25.0 (16.0 to 34.0) | 27.5 (19.5 to 30.8) | | |

**Statistical analyses**

| **Statistical analysis title** | Oral aperture |
|---|---|
| Comparison groups | PTX Tocopherol v Control no treatment |
| Number of subjects included in analysis | 25 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | = 0.161 |
| Method | t-test, 2-sided |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: All the study | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Total adverse events |

Reporting group description: -

| Serious adverse events | Total adverse events | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Total adverse events | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |

## 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