

A pharmacological protocol for the management of medication-related osteonecrosis of the jaws: A randomized study

Submission date 29/06/2023	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 06/07/2023	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 06/08/2024	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Medication-related osteonecrosis of the jaws (MRONJ) is a challenging situation in clinics. Previous studies showed that pentoxifylline (PTX) combined with tocopherol was beneficial in patients with osteoradionecrosis, due to its antioxidant and antifibrotic properties. This study aims to evaluate the effect of PTX and tocopherol in patients with MRONJ.

Who can participate?

Female Stage I MRONJ patients with osteoporosis who had developed MRONJ after tooth extractions

What does the study involve?

The test group receives the pharmacological protocol with PTX and tocopherol (2 months pre-operatively and 6 months post-operatively). The control group has sequestrectomy operations (surgical removal of necrotic bone) without any pharmacological preparation. The main outcomes are clinical healing of the mucosa after 1 month and clinical and radiographic healing of the bone lesion at 6 months.

What are the possible benefits and risks of participating?

It is expected that in osteoporosis patients with Stage I MRONJ, the proposed pharmacological treatment with PTX and tocopherol will improve mucosal and bone healing rates and minimize relapses and complications, as compared to the control group.

The drugs used in the study are safe; pentoxifylline (PTX) is a methylxanthine derivate that was originally approved by the Food and Drug Administration (FDA) to treat peripheral artery diseases and has been used to treat complications related to fibrosis for over 20 years. PTX increases vasodilation and erythrocyte flexibility and reduces blood viscosity, which leads to an improvement in peripheral blood flow and tissue oxygenation. Tocopherols are organic chemical compounds consisting of various methylated phenols with beneficial effects. Tocopherols decrease tissue fibrosis, reduce inflammation, and have antioxidant effects that protect cell membranes from lipid peroxidation by reducing the free radical damage generated during

oxidative stress. PTX in combination with tocopherol has a synergistic effect and is used for the management of osteoradionecrosis, with beneficial antioxidant and antifibrotic properties. The main risk for participants receiving the pharmacological treatment is that it is ineffective, and the chance of developing relapses or worsening the disease after the intervention remains high. No other risks other than those commonly associated with surgical intervention (e.g. post-operative bleeding, pain, swelling, infection) are foreseen.

Where is the study run from?

Department of Oral Surgery and Maxillofacial Surgery, Francesco Miulli Regional Hospital, University of Bari (Bari, Italy), and Oral Med Care srl, Regional Dental Medical Centre of Oral Surgery and Maxillofacial Surgery (Bitonto, Italy).

When is the study starting and how long is it expected to run for?

June 2013 to January 2023

Who is funding the study?

Francesco Miulli Regional Hospital (Generale Regionale Francesco Miulli) (Italy)

Who is the main contact?

Dr. Gianluca Colapinto, colapinto.gianluca@virgilio.it

Prof. Massimo Del Fabbro, massimo.delfabbro@unimi.it

Contact information

Type(s)

Principal investigator

Contact name

Dr Gianluca Colapinto

Contact details

Via Giuseppe Capaldi n 9

Bitonto

Italy

70032

+39 (0)3887913143

oralmedcaresrl@gmail.com

Type(s)

Scientific

Contact name

Prof Massimo Del Fabbro

Contact details

Department of Biomedical, Surgical and Dental Sciences, Fondazione IRCCS Ca' Granda Ospedale

Maggiore Policlinico di Milano

Via della Commenda 10

Milano

Italy

20122

+39(0)3496451220
massimo.delfabbro@unimi.it

Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

Nil known

Study information

Scientific Title

Effectiveness of a pharmacological protocol with pentoxifylline and tocopherol for the management of medication-related osteonecrosis of the jaws (MRONJ): A randomized study on 202 osteoporosis patients.

Study objectives

The aim is to verify that pharmacological treatment of preparation with pentoxifylline and tocopherol in patients affected by MRONJ and candidates for surgery, improves mucosal and bone healing rates compared to patients affected by MRONJ and candidates for surgery not undergoing pharmacological preparation.

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 13/02/2014, Institutional Review Board of the Francesco Miulli Regional Hospital (Strada Prov. 127 Acquaviva – Santeramo Km. 4, 70021, 70021 Acquaviva delle Fonti BA, ACQUAVIVA delle FONTI, 70021, Italy; +39 (0)803054111; protocollo.miulli@legalmail.it), ref: 203077-13/02/2014

Study design

Single-centre interventional randomized controlled trial

Primary study design

Other

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Medication-related osteonecrosis of the jaws (MRONJ) in osteoporosis patients

Interventions

All patients are randomly divided into two groups, a test group and a control group, in a double-blind manner. The test group will receive the pharmacological preparation with pentoxifylline (600 mg x 2/day) and tocopherol (800 IU x 1/day) from 2 months before to 6 months after the surgical procedure, while the control group will directly receive the surgical procedure. The results will be evaluated and it will be verified whether the pharmacological preparation improves the results.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Pentoxifylline, tocopherol

Primary outcome(s)

1. Mucosal healing measured clinically by visual inspection at 1 week, 2 weeks, 1 month, 2, 6, and 12 months after the intervention
2. Bone healing measured clinically and radiographically through cone beam computed tomography (CBCT) 6 and 12 months after the intervention

Key secondary outcome(s)

The following secondary outcome measures will be observed yearly from 1 year up to 8 years:

1. Stability of mucosal and bone healing measured using clinical observation of the absence of inflammatory signs and maintenance of closure without bone exposure for mucosal healing, and radiographic assessment of healthy bone with normal structure, using cone beam computed tomography (CBCT)
2. Incidences of complications, such as abscess, mucosal fistula, and phlegmon, measured throughout all the study using clinical inspection and patient's reported complaints
3. Relapses occurring when mucosal healing has occurred, but bone healing does not occur, which can lead to two scenarios:
 - 3.1. The mucosa reopens with exposure to underlying necrotic bone
 - 3.2. The mucosa remains closed, but a small fistula is created where it is possible to probe the underlying unhealed necrotic bone measured using clinical and radiographic evaluation

Completion date

31/01/2023

Eligibility

Key inclusion criteria

Patients with osteoporosis and MRONJ stage I

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

Female

Total final enrolment

202

Key exclusion criteria

1. Cancer patients with metastatic bone disease
2. Other stages of MRONJ

Date of first enrolment

01/08/2013

Date of final enrolment

01/11/2017

Locations

Countries of recruitment

Italy

Study participating centre

Department of Oral Surgery and Maxillofacial Surgery, of the Francesco Miulli Regional Hospital, University of Bari

Strada Prov. 127 Acquaviva – Santeramo Km. 4

Acquaviva delle Fonti

Italy

70021

Study participating centre

Oral Med Care srl, Regional Dental Medical Centre of Oral Surgery and Maxillo-Facial Surgery

Via Giuseppe Capaldi n 9

Bitonto

Italy

70032

Sponsor information

Organisation

Ospedale Generale Regionale Francesco Miulli

ROR

<https://ror.org/03djvm380>

Funder(s)

Funder type

Hospital/treatment centre

Funder Name

Ospedale Generale Regionale Francesco Miulli

Results and Publications

Individual participant data (IPD) sharing plan

Data analysed during the current study will be available upon request from Prof Massimo Del Fabbro (massimo.delfabbro@unimi.it)

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/07/2023	06/08/2024	Yes	No