ORTHOKINE®-THERAPY

Important information

Introduction

Orthokine® (autologous conditioned serum or ACS) is a special serum from the patients own blood, which features a significantly higher concentration of signaling proteins, especially Interleukin-1 receptor antagonist (IL-1Ra) and different growth factors.

The initial idea to develop the Orthokine®-therapy is based on the fact that Interleukin-1 (IL-1; a messenger of the immune system) plays an important role in cartilage degradation, nerve root inflammation and pain.
The opponent of IL-1, IL-1Ra, is a natural inhibitor of IL-1. Particular immune cells in the blood of a patient are capable of releasing IL-1Ra in large quantities. During the processing of Orthokine® those cells are triggered to do so as well as several growth factors, which play an important role in connective tissue repair.
Orthokine®-therapy was developed during the 1990s by Prof. (USA) Peter Wehling in Düsseldorf, Germany for the treatment of orthopaedic diseases of humans and also animals.
This therapy is successfully used by many specialists in almost 30 countries around the world. About 100,000 patients and 60,000 horses have been treated with this special biological therapy.

There are more than 30 publications on the efficacy, safety and mode of action of Orthokine®.
The effectiveness and safety of the Orthokine®-therapy has been demonstrated by clinical data from numerous physicians around the world and by results of randomised, controlled, double-blind clinical studies, published in “peer reviewed“ journals.
These data have shown that Orthokine®-therapy has significant advantages related to effectiveness and safety in comparison to a number of other recommended treatments of osteoarthritis.

Besides the use as treatment for osteoarthritis Orthokine®-therapy has particular importance in sports medicine when treating diseases of the joint or spine and sport injuries. Orthokine® is successfully used in international football and tennis as well as for the treatment of athletes in the NBA, NFL, MLB and at the Olympic Games.
The world anti doping agency (WADA) classified Orthokine® as non doping, the therapy is in accordance with the WADA guidelines.

This document is intended to give you an overview of the Orthokine®-therapy and the clinical and basic science behind it.

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A) Scientific background

Orthokine®-therapy is a conservative orthopaedic treatment based on the patient's own blood. A sample of blood is taken from the patient, incubated and separated using a special medical device (Orthokine®II or EOT®II) to produce a cell free serum containing elevated concentrations of important anti-inflammatory cytokines plus growth factors. This serum is then injected back into the same patient in a series of local injections to the affected area (for indications see studies in chapter B)). The detailed procedure of the Orthokine®-therapy has been described in several international journals (see chapter I) Literature no. 2., 4., 11., 23., 27., 33. and 34.).
Orthokine®-therapy is not an auto-haemo therapy but an autologous conditioned serum (ACS) therapy.
A number of clinical studies show that Orthokine®-therapy reduces pain and improves function, mobility and health-related quality of life. Patients can be treated safely and effectively with little side effects. No other injection therapy (e.g. corticosteroids, hyaluronic acid, PRP) rivals its long-term efficacy.
Use of Orthokine®-therapy may help to reduce the number of surgeries, the dosage and frequency of pain killing medications and therefore medical costs in the medium and long term.
Peer-reviewed articles about the Orthokine®-therapy have been published in international scientific journals.
The data, daily regular use and year long experience suggest Orthokine®-serum is an effective and well tolerated alternative to other injection therapies.

a. Basis of Orthokine®-therapy: signaling proteins (cytokines and growth factors)

The Orthokine®-therapy is based on the injection of signaling protein-rich serum (ACS). It is believed the proven efficacy of ACS is due to the synergistic effect of many of the body's own signaling proteins (cytokines and growth factors) that are present in clinically relevant concentrations in autologous conditioned serum.

Cytokines play a pivotal role in the pathogenesis of degenerative joint disease, in inflammatory conditions as well as in osteoarthritis (OA), spinal pathologies, soft tissue degeneration and in the immune system. Published scientific findings indicate that pro-inflammatory cytokines are involved in cartilage breakdown. A key role is attributed to the inflammatory Interleukin-1 (IL-1).
The therapeutic use of IL-1 inhibitors in the treatment of diseases was proposed in the 1980s and has formed the basis for the development of new biological treatment modalities.
Orthokine®-serum (ACS) contains a high concentration of interleukin-1-receptor antagonist (IL-1Ra), the natural IL-1 antagonist. Studies have shown that Orthokine®-serum, when injected locally into osteoarthritic joints, inhibits inflammation, alleviates pain and protects cartilage by improving tissue homeostasis.
Additionally, synergistic effects of IL-1Ra and other cytokines plus several regenerative growth factors are responsible for the strong and long lasting efficacy of Orthokine®-therapy.

Growth factors are tissue hormones regulating cell division, extracellular matrix production and stem cell migration. Additionally, some growth factors (e.g. TGF-ß) additionally appear to have anti-inflammatory properties. They support the necessary natural regeneration and trauma healing in musculoskeletal tissues. ACS contains PDGF, TGF-ß, IGF, FGF, EGF, HGF (see glossary) and many more growth factors. Used as single substances these factors tend to have unwanted side effects because, as single component, their dosage needs to be several orders of magnitude higher.

Used in natural combination and concentration unwanted effects of cytokines and growth factors are very rare, while often giving the same or better therapeutic effects.

B) Selection of human clinical studies

a. Orthokine®-therapy for knee osteoarthritis – University Düsseldorf (DE)

Baltzer AWA et al.: Autologous conditioned serum (Orthokine®) is an effective treatment for knee osteoarthritis. *Osteoarthritis and Cartilage* (2009) 17(2): 152-160

Aim	Evaluate Orthokine® safety and efficacy in knee Osteoarthritis vs. Hyaluronan (HA) and placebo
Quality	Randomized, prospective, placebo-controlled, double-blinded intra articular injection study
Measuring instruments	WOMAC, VAS
Number of patients	376 patients with knee osteoarthritis grades II-III
Number of treatments	6 times, twice per week. Injection volume 2 mL Orthokine®-serum
Follow up duration	24 months
Results	VAS pain reduction: 57% (Orthokine®) vs. 42% (HA) vs. 44% (placebo) $WOMAC_{global}$ improvement: 54% (Orthokine®) vs. 29% (HA) vs. 33% (placebo)
Conclusion	The Orthokine®-therapy has a long lasting efficacy of at least 2 years. It has an outstanding pain relieving effect.

b. Orthokine®-therapy for knee osteoarthritis – University Utrecht (NL)

Auw Yang KG et al.: Autologous interleukin-1 receptor antagonist improves function and symptoms in osteoarthritis when compared to placebo in a prospective randomized controlled trial. *Osteoarthritis and Cartilage* (2008) 16(4): 498–505

Aim	Evaluate Orthokine® safety and efficacy in knee Osteoarthritis vs. placebo
Quality	Multi-centre, randomized, prospective, placebo-controlled, double-blinded intra-articular injection study
Measuring instruments	KOOS, KSCRS, VAS
Number of patients	182 patients with knee osteoarthritis grades I-III
Number of treatments	6 times, twice per week. Injection volume 2 mL Orthokine®-serum
Follow up duration	12 months
Results	Significant KOOS symptom reduction: Orthokine® vs. placebo Significant KOOS sport reduction: Orthokine® vs. placebo
Conclusion	Autologous interleukin-1 receptor antagonist improves function and symptoms in osteoarthritis when compared to placebo in a prospective randomized controlled trial

c. Orthokine®-therapy for low back pain – University Bochum (DE)

Becker C et al.: Efficacy of epidural perineural injections with autologous conditioned serum for lumbar radicular compression: an investigator-initiated, prospective, double-blind, reference-controlled study. *Spine* (2007) 32(17): 1803–1808

Aim	Test Orthokine® safety and efficacy for low back pain vs. Triamcinolon 5 mg (T5) and 10 mg (T10)
Quality	Randomized, prospective, controlled, double-blinded epidural-perineural injection study
Measuring instruments	Oswestry, VAS
Number of patients	84 patients with chronic radiculopathy
Number of treatments	3 times, once per week. Injection volume 2 mL Orthokine®-serum only, Triamcinolon: local anaesthetic 1 mL + 1 mL
Follow up duration	6 months
Results	VAS pain reduction: 70% (Orthokine®) vs. 53% (T5) vs. 60% (T10)
Conclusion	The Orthokine®-therapy has a long lasting efficacy of at least 6 months

d. Orthokine®-therapy of muscle lesions in athletes – Deutsche Sporthochschule, Köln (DE)

Wright-Carpenter T et al.: Treatment of muscle injuries by local administration of autologous conditioned serum: a pilot study on sportsmen with muscle strains. *Int J Sports Med* (2004) 25(8): 588–593

Aim	Test Orthokine® safety and efficacy for muscle strains in Pro-athletes vs. Traumeel/Actovegin (T: 2 mL + A: 3 mL) combination
Quality	Randomized, prospective, controlled, intra lesional injection study
Measuring instruments	MRI, time until return to full training
Number of patients	84 patients with chronic radiculopathy
Number of treatments	Orthokine® 5.4 times, T/A 8.3 times, every 2nd day. Orthokine®-serum was diluted 1:2 with saline. Injection volume 5 mL (1 mL each in 5 injection points covering the injury)
Follow up duration	6 weeks
Results	Reduced time to return to full training: 30% (Orthokine® vs. T/A)
Conclusion	The Orthokine®-therapy has a statistically significant faster regenerative effect on muscle strains compared to T/A

e. Orthokine®-therapy after ACL reconstruction – University Zagreb (HR)

Darabos N et al.: Intraarticular application of autologous conditioned serum (ACS) reduces bone tunnel widening after ACL reconstructive surgery in a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* (2011) 19: 36-46

Aim	Test Orthokine® safety and efficacy for tibial bone tunnel widening vs. placebo in post ACL plasty injection treatment
Quality	Randomized, prospective, controlled, intra articular injection study
Measuring instruments	CT bone tunnel measurement, time until return to full training
Number of patients	62 patients with single bundle ACL plasty
Number of treatments	4 times. Time points after surgery day 0, 1, 6, 10
Follow up duration	12 months
Results	Statistically significant reduction of bone tunnel width: Orthokine® vs. placebo
Conclusion	The Orthokine®-therapy has a statistically significant effect on post ACL plasty occurring bone tunnel widening

f. Orthokine®-therapy prevents surgery in knee OA – Hospital Ruber Internacional, Madrid (ES)

Baselga J and Hernandez PM: ORTHOKINE-Therapy for high-pain knee osteoarthritis (OA) may delay surgery. Independent 2 year case follow-up. ICRS congress 2013, Izmir, Turkey

Aim	Test long term Orthokine®-therapy safety and efficacy for severely symptomatic knee osteoarthritis
Quality	Independent prospective intra-articular injection study
Measuring instruments	WOMAC, VAS
Number of patients	118 patients with knee OA grades I-IV
Number of treatments	Orthokine®-serum 4 times, once per week. 30 sessions of physiotherapy starting 4 weeks after injections.
Follow up duration	24 months
Results	Statistically and clinically significant reduction of all scores >55%, no statistically significant difference as per OA grade
Conclusion	The Orthokine®-therapy has an outstanding statistically and clinically significant long lasting effect on severely symptomatic knee OA. It may postpone joint surgery.

g. Orthokine®-therapy for hip osteoarthritis – Orthopädische Praxis Königsallee, Düsseldorf (DE)

Baltzer AWA et al.: A new treatment for hip osteoarthritis: clinical evidence for the efficacy of autologous conditioned serum. *Orthop Rev* (2013) 5(2):e13

Aim	Test Orthokine®-therapy efficacy for hip osteoarthritis
Quality	Independent retrospective intra-articular injection study
Measuring instruments	VAS
Number of patients	119 patients with hip OA grades II-IV
Number of treatments	3 groups: Orthokine® (5.9 times) vs. Orthokine® (5.7 times) + Cortisone (1.9 times) vs. Orthokine® (5.9) + Cortisone (2.9 times) + rhIL-1Ra (3.5 times)
Follow up duration	14 months
Results	Statistically significant reduction of VAS in all 3 groups, no statistically significant difference as per treatment modality or OA grade.
Conclusion	The Orthokine®-therapy has a statistically and clinically significant effects on hip OA, can possibly prevent, or at least delay surgery

C) Selection of animal studies

a. Orthokine®-therapy for equine lameness – University Colorado State (US)

Frisbie DD et al.: Clinical, biochemical, and histologic effects of intra-articular administration of autologous conditioned serum in horses with experimentally induced osteoarthritis. *Am J Vet Res* (2007) 68(3): 290–296

Aim	Test Orthokine® safety and efficacy for equine experimentally induced front limb metacarpal OA
Quality	Randomized, prospective, placebo-controlled, intra-articular injection study
Measuring instruments	Lamness scoring (0-5), cartilage and synovium histology, intra-articular fluid IL-1Ra measurements
Number of patients	16 healthy equine patients. 8 horses per group
Number of treatments	4 times, days 14, 21, 28, 35 after insult
Follow up duration	70 days
Results	Statistically significant less lameness in Orthokine®-serum vs. placebo. Intra-articular IL-1Ra concentration significantly elevated vs. placebo
Conclusion	The Orthokine®-therapy improves lameness and synovial hyperplasia in experimentally induced front limb metacarpal OA

b. Orthokine®-therapy for equine lameness – University Berlin (DE)

Jöstingmeier U: Vergleichende Betrachtung des Behandlungserfolges der intraartikulären kombinierten Behandlung mit Natriumhyaluronat und Betamethason mit der intraartikulären Behandlung mit autologem konditionierten Serum (IL-1Ra) bei Pferden mit positiver Hufgelenksanästhesie - Eine Anwendungsbeobachtung. *Inaugural-Dissertation* an der Freien Universität Berlin (2008) ISBN 978-3-86664-665-0

Aim	Test Orthokine®-serum efficacy for front limb coffin joint injection treatment vs. Hyaluronan (HA) plus Betamethason (Corticosteroid)
Quality	Prospective, controlled, intra-articular injection study
Measuring instruments	Lameness score 0-5
Number of patients	54 patients
Number of treatments	Orthokine®-serum 3 mL 3-7 times every 7-14 days. HA+B initial 4 mL and 1-5 further HA injections 7-10 days apart.
Follow up duration	6 months
Results	Statistically significant improvement Orthokine®-serum (88.9% of patients lame free) vs. control (63% of patients lame free)
Conclusion	The Orthokine®-therapy has a statistically significant effect on front limb coffin joint lameness

c. Orthokine®-therapy for equine lameness – University Uppsala (SE)

Österdahl J: Evaluation of autologous conditioned serum. Degree project 2008:67 at Swedish University of Agricultural Sciences, Uppsala (2008) ISSN 1652-8697

Aim	Test Orthokine®-serum in equine cases of coffin and fetlock lameness that did not respond to treatment with HA (Hyonate®) or PSGAG (Adequanin®)
Quality	(Retro)prospective, intra-articular injection study
Measuring instruments	Lameness score 0-5 / back to sport
Number of patients	20 patients. 10 HA failures, 10 PSGAG failures
Number of treatments	Presumably 3-4 á 2 mL weekly. Number according to established protocol
Follow up duration	Evaluation only “back to sport“, no data on duration
Results	In 7/10 or 10/10 cases therapeutic success with Orthokine®-serum for equine degenerative joint disease therapy failures with Hyonate® or Adequanin®
Conclusion	The Orthokine®-therapy is a valuable tool for refractory lameness cases

d. Orthokine®-therapy for muscle lesions in mice – CNRS Paris (FR)

Wright-Carpenter T et al.: Treatment of muscle injuries by local administration of autologous conditioned serum: animal experiments using a muscle contusion model. *Int J Sports Med* (2004) 25(8): 582–587

Aim	Test the effect of Orthokine®-serum on the muscle regeneration process in a defined muscle contusion injury (steel ball drop from 100 cm)
Quality	Controlled laboratory study
Measuring instruments	Histology
Number of patients	108 syngenic C57 Bl/6 mice
Number of treatments	Orthokine®-serum and placebo 10 µL each. 3 injections at 2 hrs, 24 hrs, 48 hrs
Follow up duration	35 days
Results	Statistically significant more (≤2x) activated satellite cells in Orthokine®-serum group vs. saline at 30 and 48 hrs. Statistically significant more CN fibers (87.4% vs. 60.3%) at day 6-8.
Conclusion	At day 7 the treatment has accelerated the healing process. The regenerating myofibers are comparatively more mature. No difference between groups at day 14. ACS treatment appears to be a powerful tool for the treatment of muscle contusion injuries.

e. Orthokine®-therapy for Achilles tendon lesions in rats – University Harvard (US)

Majewski M et al.: Accelerated Healing of the Rat Achilles Tendon in Response to Autologous Conditioned Serum. *The American Journal of Sports Medicine* (2009) 11: 2117-2125

Aim	Test the effect of Orthokine®-serum on the healing of transected and resutured rat Achilles tendon
Quality	Controlled laboratory study
Measuring instruments	Histology, biomechanical testing, rtPCR
Number of patients	Eighty adult male Sprague Dawley rats
Number of treatments	Orthokine®-serum and placebo 170 µL each. 3 injections at 24 hrs, 48 hrs, 72 hrs
Follow up duration	8 weeks
Results	More rapid recovery of the normal histologic appearance of the tendon tissue in response to ACS. >10x higher Col I mRNA expression vs. placebo
Conclusion	The Orthokine®-therapy has a statistically significant effect on Achilles tendon healing

f. Orthokine®-therapy for Achilles tendon lesions in rats – University Basel (CH)

Heisterbach PE et al.: Effect of BMP-12, TGF-β1 and autologous conditioned serum on growth factor expression in Achilles tendon healing. *Knee Surg Sports Traumatol Arthrosc* (2012) 20(10): 1907-1914

Aim	Test the role of growth factors during tendon healing in a rat model and their reaction to single and multiple growth factor treatment
Quality	Controlled laboratory study
Measuring instruments	Immunohistology
Number of patients	Sixty male adult Sprague-Dawley rats
Number of treatments	Orthokine®-serum 170 µL each. 3 injections at 24 hrs, 48 hrs, 72 hrs
Follow up duration	8 weeks
Results	Orthokine®-serum had the strongest effect on growth factor expression. It increased bFGF significantly after 8 weeks compared to controls (P = 0.007) and BMP-12 (P = 0.004). A nearly significant elevation of bFGF was also observed with ACS in week 4 compared to BMP-12 (P = 0.074) and TGF-b (P = 0.084)
Conclusion	The present study suggests that the 1st week of tendon healing is a crucial period of growth factor stimulation. ACS has the greatest influence on later expression especially of bFGF and BMP-12

D) Selection of in vitro studies

a. Orthokine® comparison with ACP plasma – University of Applied Sciences Bonn-Rhein-Sieg (DE)

Weisshaar MP, Gaji S: Signaling Proteins (Growth Factors and Cytokines) in Orthopaedics. Comparison of two blood processing techniques: ORTHOKINE® and ACP®. CORS congress 2013 Venice, Italy

Aim	Test the content of growth factors and cytokines in Orthokine®-serum compared to ACP plasma
Quality	Controlled laboratory study
Measuring instruments	ELISA
Number of patients	9 healthy volunteers
Measured parameters	Orthokine®-serum, ACP plasma, baseline blood
Follow up duration	1 day
Results	Orthokine®-serum had higher content of almost all signaling proteins measured. In particular, IL-1Ra was 6.6 fold over ACP.
Conclusion	Orthokine®-serum possibly has a higher clinical efficacy than ACP due to higher concentration of clinically relevant signaling proteins.

E) Contraindications and side effects

There are no known incompatibilities between Orthokine®-ACS and other drugs such as NSAID. However, the usual points relating to intra-articular and spinal injections apply:

- Special care should be taken in case of insufficient hemostasis (e.g. in case patients take systemic anti-coagulants) when taking blood and when re-injecting serum into the patient (hemarthrosis).

Orthokine®-ACS should not be pre-mixed with other compounds. In particular local anaesthetics may have a negative effect on the proteins in Orthokine®-ACS. Additionally, there is information in the literature that some local anaesthetics may be chondrotoxic.

About the treatment with Orthokine®-ACS during pregnancy and lactation or in infants and children no informations are available.

Only limited information is available in cases of rheumatoid arthritis and psoriasis arthritis. Patients may profit, however no study data exist.

No positive or negative documentation exists regarding co-morbidities such as cancer, diabetes, chronic infections (e.g. HIV, Hepatitis, Herpes).

Orthokine®-ACS is 100% autologous material. It is used for local injections. Unwanted effects have been observed very rarely at the same frequency as in placebo injection (physiologic saline).

- Unwanted effects include pain, heat and swelling (flares) at the injection site with a total frequency of 1.3% as determined in a study by Baltzer et al. in 2009.
- Flares following joint injections are usually treated with NSAID and topical cooling of the joint. They usually occur within 6 hrs after injection and abate within 24 hrs. A low dose corticosteroid injection may be considered should a flare persist.

Although Orthokine®-ACS is very safe, intra-articular infection is a general risk with intra-articular injections and needs to be treated accordingly without any delay. As an obligatory rule Orthokine®-ACS should only be injected when filtered through a 0.2 µm filter. No infections or systemic side effects caused by Orthokine®-ACS have been observed. As of January 2014 more than 100,000 patients have been treated with approx. 400,000 Orthokine®-ACS injections.

The only observed intra-articular infect after Orthokine®-ACS injection occurred in a clinical study in the Netherlands by Auw Yang et al. It was found to have been caused by the injection technique.
The usual points of care concerning transfusion-relevant infections should always be obeyed. Blood aspiration for Orthokine®-ACS therapy should not be performed if a patient has an acute, symptomatic infection.

F) Medical devices EOT®II and Orthokine®II

The Orthokine®-syringe (EOT®II and Orthokine®II) is a medical device bearing the CE mark (equivalent to a FDA medical device approval). EOT®II (10 mL) and Orthokine®II (50 mL) are systems for blood sampling, incubation and processing for treatment with autologous components.

Both syringes contain medical grade glass spheres with defined surface, shape and structure. They are produced in a highly controlled multi stage process.
During the incubation of the patient's blood these glass spheres induce a significant increase in production of cytokines, especially IL-1Ra and growth factors.
In numerous laboratory experiments the ideal parameters were defined to provide a therapeutically effective serum.
This process is patented.

The special syringes used to safely process the serum are produced in accordance with the regulatory requirements for medical devices (CE mark). All Orthokine® special syringes undergo very strict quality control that ensures that patients' safety is never at risk.

G) Regulatory environment

a. Legal framework

The Orthokine®-therapy is administered under the established physicians freedom of treatment. The processed ACS is an individual drug. By German “Arzneimittelgesetz” (AMG), physicians may produce ACS for the purpose of treating their own patients (AMG §§4a, b). The Orthokine®-therapy is not a drug to sell, it is a service provided by the physician. For every country this legal framework needs to be evaluated separately.
Legislations with respect to organ transplants (German Transplantation Act) and transfusions (German Transfusion Act) do not apply.

Before applying the Orthokine®-therapy, it is of the utmost importance that all practice/clinic staff who will be working with the system receives proper training. The training is documented and is an integral aspect of the establishment and maintenance of an obligatory on-site quality assurance system.

b. Doping related regulations

Since “THE 2010 PROHIBITED LIST“ WADA (World anti doping agency) has liberalised the use of blood products such as Orthokine® (“blood spinning”) therapy for intra-articular, tendon and tendon attachment. Orthokine®-therapy is regarded not doping. WADA however prohibits the use of the recombinant synthetic version of the growth factors present in Orthokine®-ACS.

You can find the related information on the following web site:
- www.wada-ama.org
- click on “Prohibited List” in the Quick Links section
- click on “Q&A on 2014 Prohibited List”
- click on “What is the status of platelet derived preparations (PRP)?”

H) Distribution

In Germany Orthokine® (EOT®II and Orthokine®II) syringes are distributed by:

ORTHOGEN Lab Services GmbH
Graf-Adolf-Str. 41
40210 Düsseldorf
Germany

T +49 (0)211 38 700 700
info@orthokine.com
www.orthokine.com

Currently the products is also available in following countries:

- Australia
- Austria
- Bosnia and Herzegowina
- Colombia
- Croatia
- Cyprus
- Czech Republic
- Estonia
- Finland
- Israel
- Italy
- Kosovo
- Latvia
- Lithuania
- Macedonia
- Montenegro
- New Zealand
- Poland
- Portugal
- Romania
- Russia
- Serbia
- Slovakia
- Slovenia
- Spain
- Switzerland
- Taiwan
- Turkey

The distribution partners of Orthogen Lab Services GmbH are responsible for all activities in these countries.

I) Literature

Published studies relevant for Orthokine® (partial list, alphabetical order):

1. Alvarez-Camino JC et al.: Use of autologous conditioned serum (ORTHOKINE) for the treatment of the degenerative osteoarthritis of the temporomandibular joint. Review of the literature. *Med Oral Patol Oral Cir Bucal* (2013) 18 (3):433-438
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J) Glossary

ACL-plasty:	replacement of the torn anterior cruciate ligament with another ligament
BMP:	bone morphogenetic protein
Corticosteroids:	cortisone
EGF:	epithelial growth factor
FGF:	fibroblast growth factor
HGF:	hepatocyte growth factor
Hyaluronan:	hyaluronic acid
IGF:	insulin-like growth factor
IL-1:	interleukin-1. Signaling protein crucially involved in inflammation and tissue destruction
IL-1Ra:	interleukin-1 receptor antagonist. Signaling protein competitively inhibiting IL-1
NaCl:	sodium chloride
NSAID:	non steroidal anti inflammatory drugs
PDGF:	platelet derived growth factor
Placebo:	substance without clinical effects, used in clinical science and treatment
PRP:	platelet-rich plasma (platelets concentrated >3 fold in their own plasma)
PSGAG:	polysulfated glycosaminoglycan
RCT:	randomized, controlled, double-blind clinical studies
Signaling proteins:	proteins such as cytokines and growth factors with a hormone like effect on other cells
synovial hyperplasia:	swelling and inflammation of the inner surface of the joint capsule
TGFß:	transforming growth factor
tissue homeostasis:	physiological equilibrium of the biological system „joint“
VAS:	visual analog scale
WADA:	world anti doping agency
WOMAC:	Western Ontario and McMaster Universities Arthritis Index