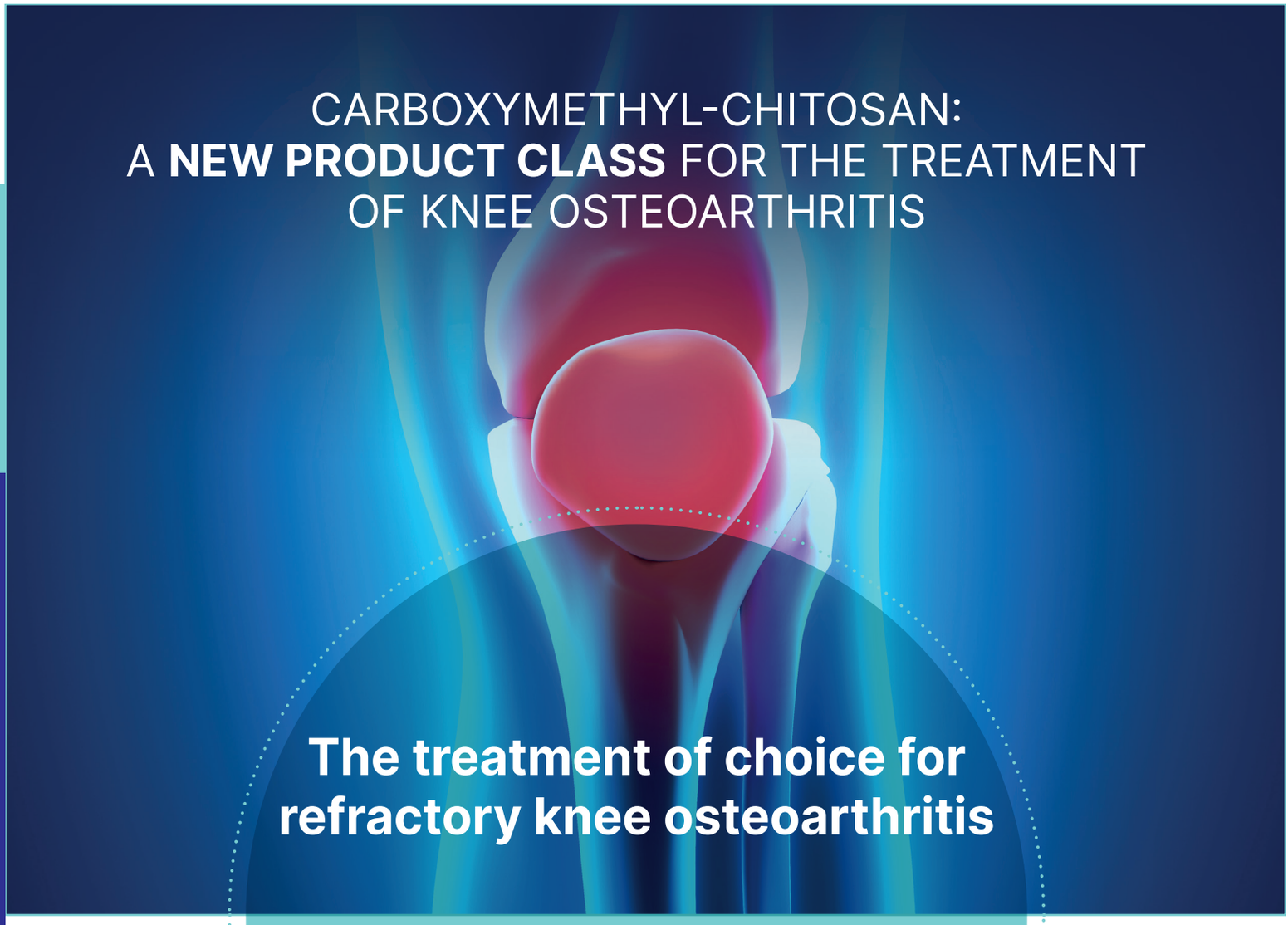
CARBOXYMETHYL-CHITOSAN: A **NEW PRODUCT CLASS** FOR THE TREATMENT OF KNEE OSTEOARTHRITIS



The treatment of choice for refractory knee osteoarthritis

Unique, single-injection fluid implant

BELGIAN TECHNOLOGY

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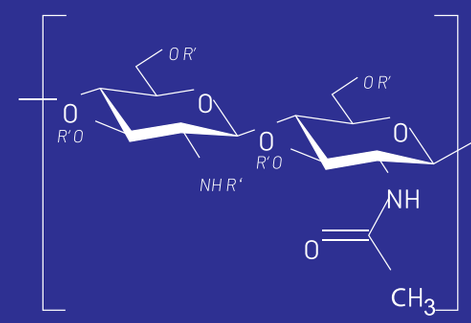
HOSPITAL INNOVATIONS

A true innovation in the treatment of knee osteoarthritis...

KioMedine[vs]one is a unique fluid implant indicated for the symptomatic treatment of knee osteoarthritis with a single intraarticular injection. **KioMedine[vs]one** is based on a world-first, exclusive, animal-free **KioMedine® (CM) Carboxymethyl-Chitosan.**

KiOmedine® CM-Chitosan is a highly purified polysaccharide derived from *Agaricus Bisporus* (button mushroom) resulting from years of research and innovation and is a patented technology[1,2], manufactured by KiOmed Pharma in Belgium.

Thanks to a unique structure that differs from natural chitosan, **CM-Chitosan** provides to **KioMedine[vs]one** an exclusive dual mechanism of action to tackle osteoarthritis pain and other symptoms by enhancing joint lubrication and by reducting oxidative stress (protection)[3,4].



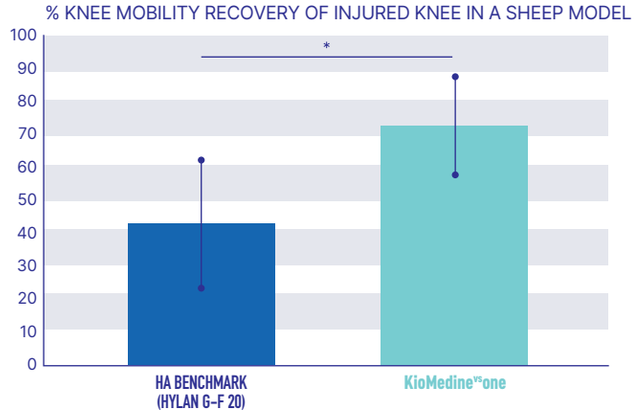
R'= -H or - R-COOH

CM-Chitosan, a polymer of glucosamine units

Lubricating properties

KioMedine[vs]one significantly improves the lubricating properties and reduces the coefficient of friction of osteoarthritis synovial fluid[4].

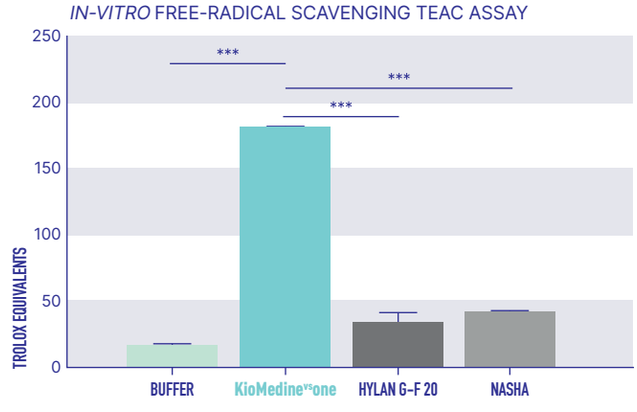
KioMedine[vs]one showed a significant recovery of joint motion in an animal ex-vivo model versus the recovery capacity of a crosslinked HA benchmark.



Free-radical scavenging capacity

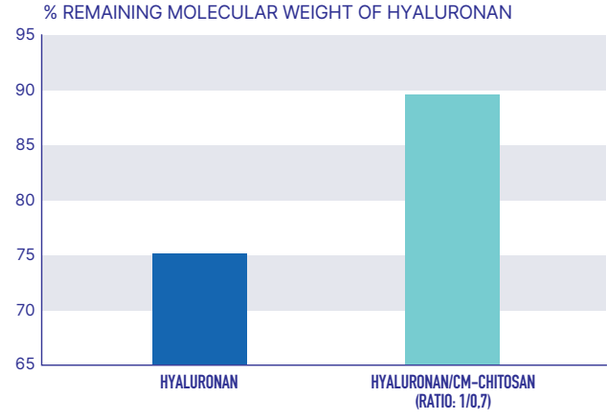
Due to its intrinsic free-radical scavenging capacity, **KioMedine[vs]one** contributes to the protection of endogenous synovial components from oxidative stress[4].

KioMedine[vs]one showed significantly superior free radical scavenging capacity compared to crosslinked HA benchmarks in a Trolox equivalent antioxidant capacity (TAEC) assay.



Hyaluronic acid protection capacity

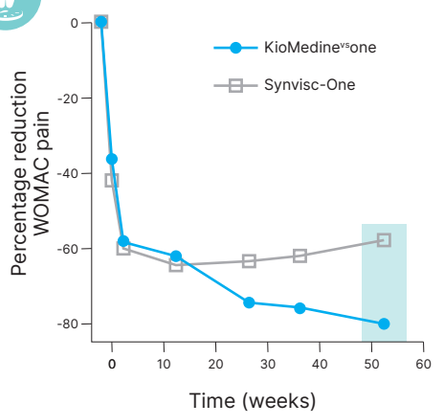
KioMedine[vs]one contributes to the **protection of endogenous synovial components** (Hyaluronic acid) from oxidative stress by capturing free radicals.



KioMedine^{vs}one demonstrates **73.5% pain reduction score** with **high responder rate up to 12 months** in refractory OA patients

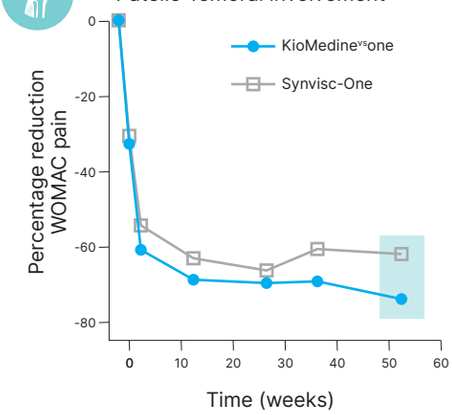
2024 PIONEER – randomised control trial. 12 months safety and performance of KioMedine^{vs}one in refractory OA patients[9]

Obese (BMI > 30 kg/m²)



Δ **-21.7%** at 12M

Overall population / Patello-femoral involvement



Δ **-11.5%** at 12M

104 patients of which **>75%** were eligible for TKR

100% of patients had patello-femoral involvement and **75%** of patients had tricompartmental OA

No new signal related to safety was observed as compared to the previous clinical data

73.5% mean reduction in WOMAC pain score at 12 months

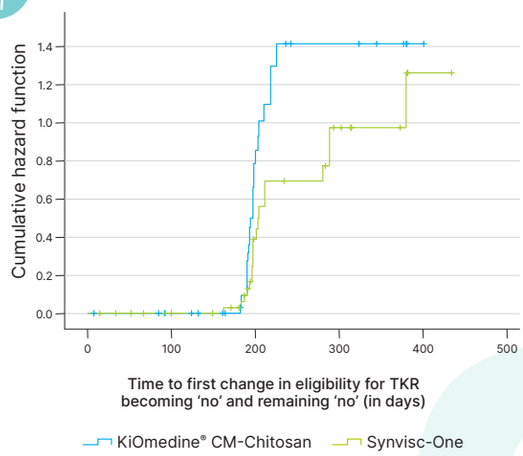
Increasing KioMedine^{vs}one responder rate with time, reaching **93.8%** at 12 months

>90% physician and patient satisfaction at 12 months for KioMedine^{vs}one vs. 66% physician and 79% patient satisfaction for Synvisc-one

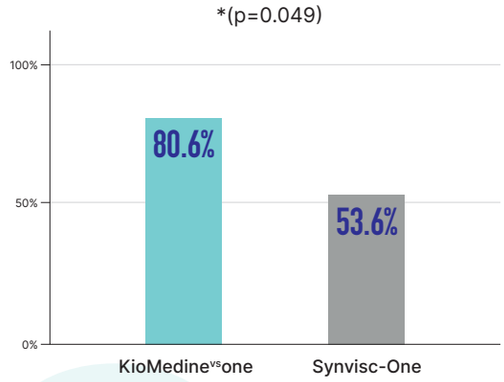
KioMedine^{vs}one showed **clinically important differences with superior trends in the reduction of pain scores** in patello-femoral, obese and TKR candidates

80.6% of TKR eligible candidates had postponed surgery after KioMedine^{vs}one injection

Time to change to non-eligibility to TKR



Percentage of patients with postponed TKR at 9 months *(p=0.049)

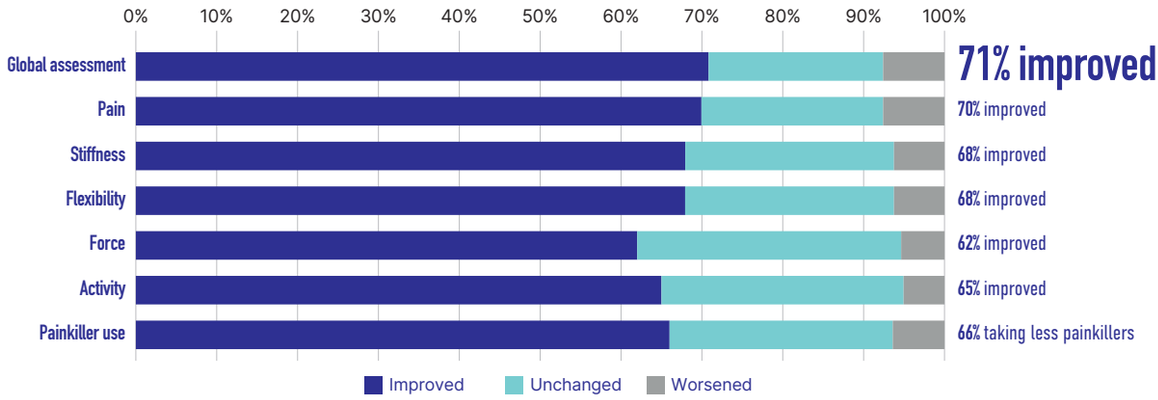


KioMedine^{vs}one demonstrated a **significantly higher probability of rendering patients non-eligible for TKR** at 9 months, showing rates of 80.6% compared to 53.6% (p=0.049). Additionally, patients **experienced a longer time until TKR.**

A total of 370 patients included in different clinical studies

In real-life injections, KioMedine[vs]one showed on average 16 months improvement in refractory OA patients[8]

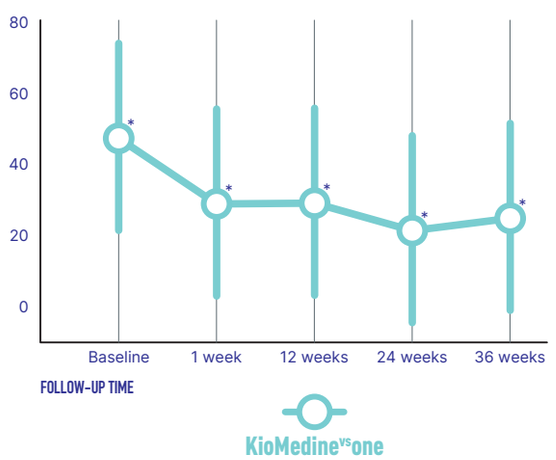
Long-term data were analyzed for **66 injections in 62 refractory knee OA patients**.
Mean follow-up time after injection: **16.4 months** (SD=10, min=4.3, max=35.7 months)



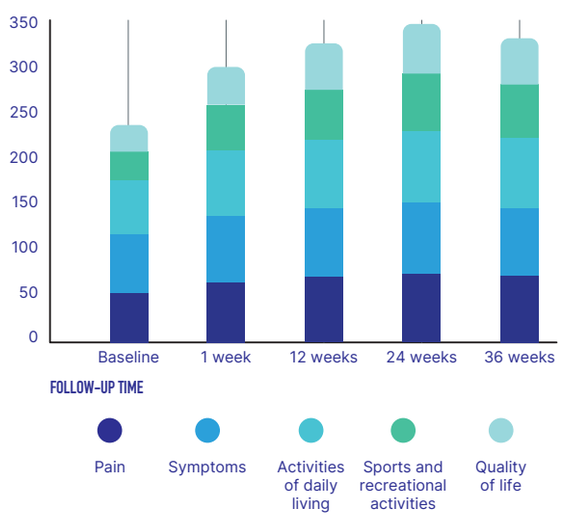
➔ **70%** of the patients reported considering an additional injection if needed

In real-world setting, KioMedine[vs]one showed rapid pain relief in 1 week, lasting at least 9 months[7]

Mean VAS pain score



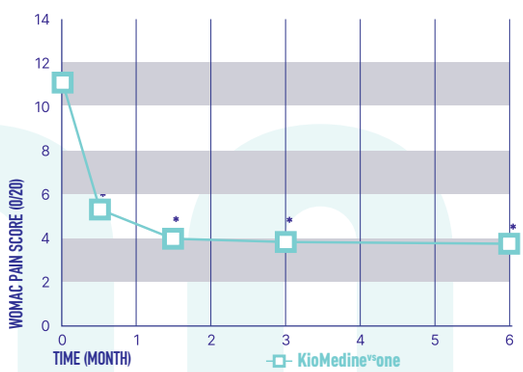
KOOS (Knee Injury and Osteoarthritis Outcome Score) scores



➔ 50 patients with KLII and III
➔ Mean BMI 30.1Kg/m² +/-7.0
➔ **80%** of patients had a KOOS pain score improvement at 9 months

6 months proven safety and efficacy on symptomatic knee OA (APROOVE clinical trial)[5,6]

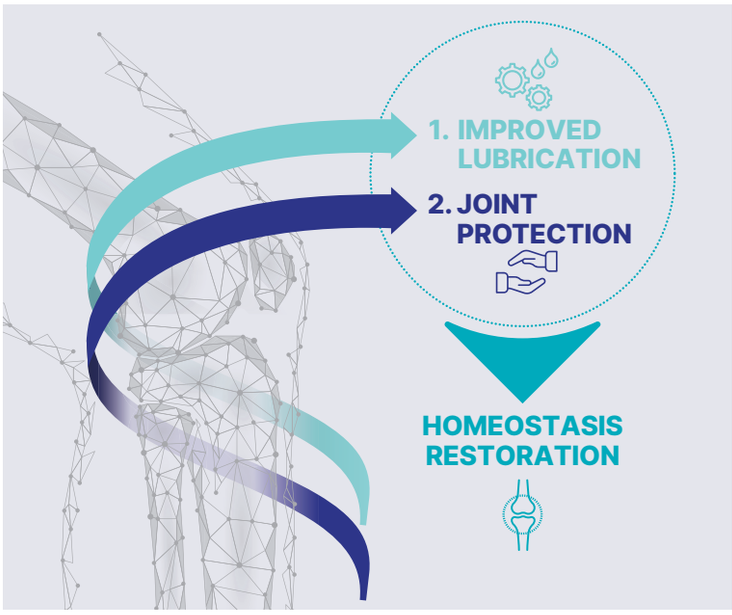
EVOLUTION OF WOMAC PAIN SCORE (stage 2, Per-Protocol cohort, ANOVA for repeated measures, *p<0,0001)



➔ 63 patients with KL II/III, of which some were obese
➔ Rapid onset on action in **2 weeks**
➔ Reduction of WOMAC pain score by **66%** and significant reduction of all OA symptoms for at least **6 months**
➔ High responder rate of **76%**
➔ **90%** physician and **86%** patient satisfaction at 6 months

KioMedine[vs]one has two key properties leading to a better quality of life for OA patients

UNIQUE DUAL MECHANISM OF ACTION



1. Improved joint lubrication

Cartilage reduces friction by forming fluid films or boundary layers that protect surfaces during movement. CM-Chitosan enhances this protection by cooperating with natural lubricants, like lubricin, to form an additional layer over the cartilage. Its unique structure significantly improves joint lubrication, leading to smoother movement with less pain and stiffness for patients.

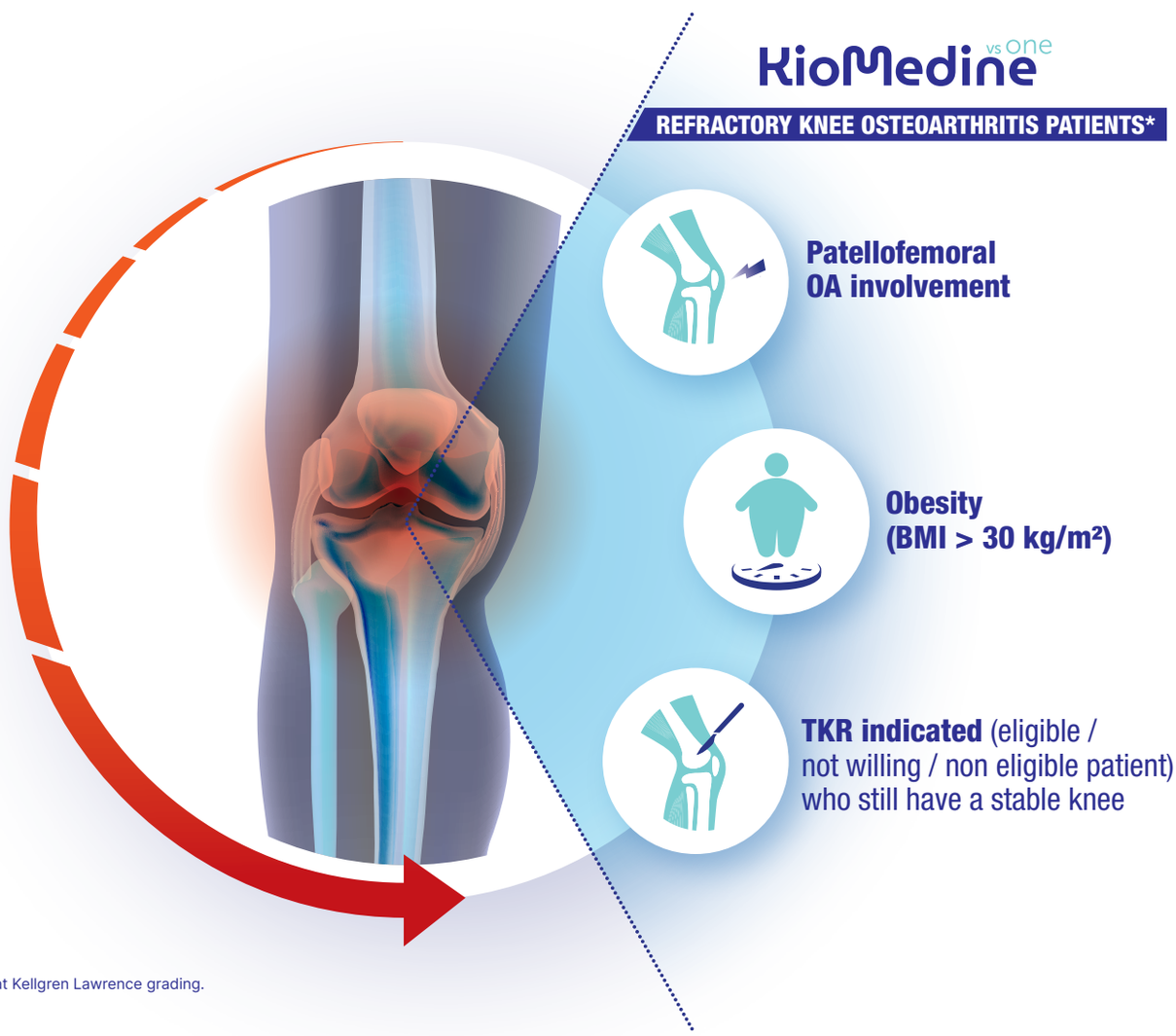
2. Unique protection against joint damage

CM-Chitosan offers unique protection against joint damage thanks to its carboxymethyl functional groups. These groups effectively neutralise the harmful free radicals associated with oxidative stress, which occurs naturally during the development of osteoarthritis. This protection interferes to slow the inflammation in osteoarthritis and the irreversible degradation of endogenous hyaluronic acid caused by oxidative stress.

Restoring homeostasis in the joint

CM-Chitosan has a positive effect on the cellular environment inside the joint, disrupting the vicious cycle of osteoarthritis. With its unique properties, CM-Chitosan interrupts the self-perpetuating vicious cycle of osteoarthritis, enabling patients to regain a better quality of life.

THE TREATMENT OF CHOICE FOR REFRACTORY OA PATIENTS



* No matter what Kellgren Lawrence grading.

KioMedine^VS one composition

- *KioMedine^VS one contains a sterile, non-pyrogenic, viscous solution composed of non-animal, linear (i.e. non-crosslinked) carboxymethyl chitosan buffered in an isosmotic condition. The 3 ml volume of KioMedine^VS one is suitable for one injection into the knee. KioMedine^VS one is a bioabsorbable implant that must be injected by an authorized physician experienced in intraarticular injections.*

KioMedine^VS one is highly biocompatible and shows a good overall safety profile in clinical practice

- No serious or unanticipated adverse event or patient withdrawal related to the safety of the treatment was reported during clinical investigations.
- Treatment related adverse events (TRAE) were transient, post-injection self limiting local effects.
- The onset of such adverse events is generally a few hours after the injection. The intensity may vary depending on other pre-existing unrecognised joint conditions (such as undetecting underlying inflammatory conditions, gout, chondrocalcinosis, etc.) and on individual patient's pain threshold.
- Anticipate the possible occurence of post-injection pain by informing the patient and by suggesting remedial temporary treatment if necessary.
- The TRAE had no impact on short and long-term clinical performance of Kiomedine^VS one intra-articular injection.

Most frequent transient and self-limited TRAEs	CM-Chitosan
Arthralgia	25.4%
Joint effusion	6.3%
Joint swelling	6.3%
Synovitis / Arthritis	4.8%

Reference clinical study APROOVE

Contraindications

For intraarticular use only. Do not inject KioMedine^VS one in patients who have a known allergy or hypersensitivity to any of the product components, infections or skin disease at or around the injection site, severe inflammation, synovitis or arthritis of the knee joint, a history of autoimmune and crystal diseases, evidence of lymphatic or venous stasis or serious blood disorders.

Warnings and Precautions

The safety and performance of KioMedine^VS one have not been established in conditions other than osteoarthritis of the knee.
The injection carries a risk of infection. Strict adherence to aseptic conditions is required to avoid joint infection. Use of an appropriate disinfectant is required for skin preparation before injecting the contents. Do not use quaternary ammonium disinfectants for skin preparation as KioMedine^VS one may precipitate in their presence. KioMedine^VS one should not be injected in case of any suspected joint effusion prior to the injection.

Most frequent adverse events

Temporary joint pain, arthralgia, joint effusion, joint swelling, joint stiffness, joint warmth, injection site pain or synovitis of the treated joint. Acute synovial inflammation characterised by significant painful effusion of the knee, and possibly low-grade fever, can also occur following the intra-articular injection of KioMedine^VS one.

For more information about adverse events and contraindications, please refer to the instructions for use provided with the package unit.

KiOmed PHARMA

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About KiOmed Pharma

Capitalizing on a history of innovation and expertise in exclusive natural chitosan chemistry, KiOmed Pharma develops a unique pipeline of medical devices that addresses unmet medical needs in high-impact pathologies and major social burdens such as invalidating osteoarthritis, skin aging and ophthalmology.

For safety concerns and incident reports please contact our medical device vigilance department immediately (e-mail: vigilance-rheumatology@kiomedpharma.com).

References

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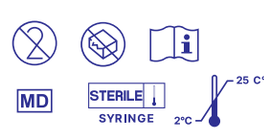
7. Nils A. Lynen, Christoph Eichhorn, Nicolas Portelange, Mickaël Chausson, Wim Weyenberg Rheumatology and Therapy. 2024 Jun;11(3):649-662.
8. Van Overschelde P, Chausson M, Portelange N, Schifflers M. CM-Chitosane dans l'arthrose avancée du genou : Bénéfices prometteurs à long terme apres une seule injection intra-articulaire (poster SFR 2023).
9. Data on file.

Product code: UDI-DI: 05404023514004



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