PRODUCT INFORMATION

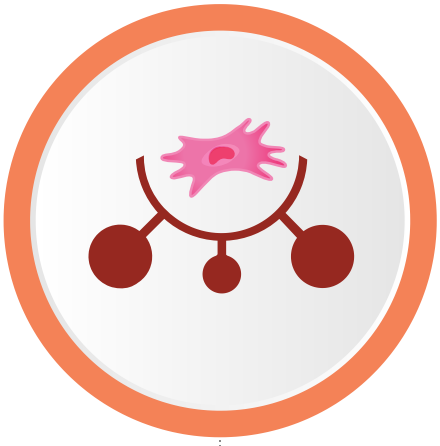
Introducing StemOne™

A first-in-class, standardized, off-the-shelf, allogeneic mesenchymal stem cell therapy, approved by the Drug Controller General of India(DCGI), for use in the management of Grade II and Grade III knee OA

Advantages of mesenchymal stem cells[1]

Abundance and ease of isolation

Can be isolated from various tissues in the body, but the bone marrow and subcutaneous adipose tissues remain the preferential sources of obtaining MSCs, due to their relative abundance



Multilineage differential potential

Have the potential to differentiate into various cell types like osteocytes, chondrocytes, and adipocytes

Immunomodulatory properties

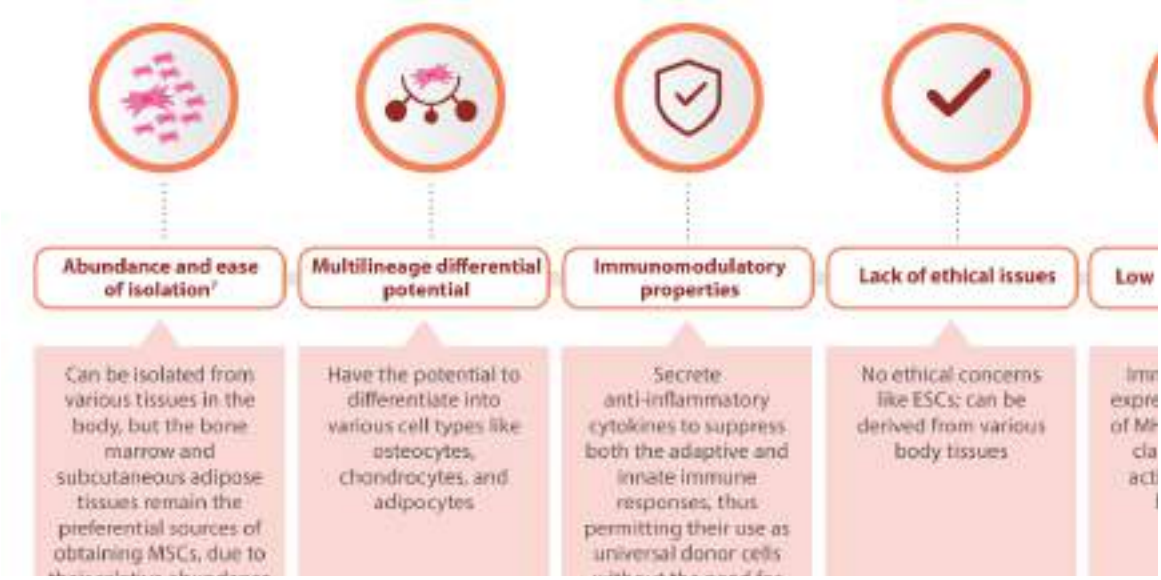
Secrete anti-inflammatory cytokines to suppress both the adaptive and innate immune responses, thus permitting their use as universal donor cells without the need for immunosuppressants

Lack of ethical issues

No ethical concerns like ESCs; can be derived from various body tissues

Low immunogenicity

Immunoprivileged; express very low levels of MHC class I, no MHC class II and do not activate allogeneic lymphocytes



Dose[2]
In non-obese patients with grade 2 & 3 knee OA (BMI<30kg/m2)
Single intra-articular dose of allogeneic mesenchymal stem cells , 25 million cells suspended in 1 ml CryoStor CS5® plus 1 ml Plasmalyte-A, followed by 2 ml Sodium hyaluronate injection

Storage
−185°C to −196°C

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Mechanism of action

StemOne™ leads to cartilage repair and regeneration via three mechanisms.[3,4,5]

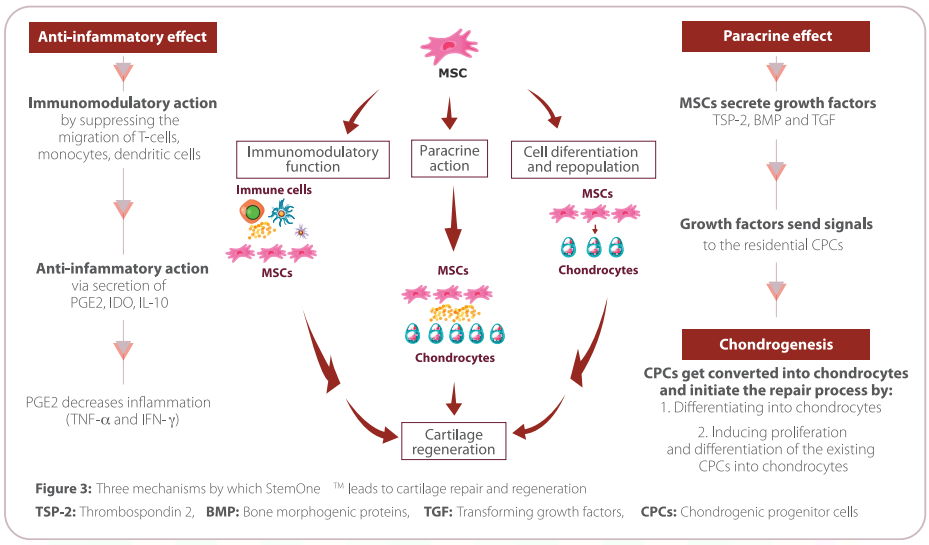

Figure 3: Three mechanisms by which StemOne ™ leads to cartilage repair and regeneration

TSP-2: Thrombospondin 2, **BMP:** Bone morphogenic proteins, **TGF:** Transforming growth factors, **CPCs:** Chondrogenic progenitor cells

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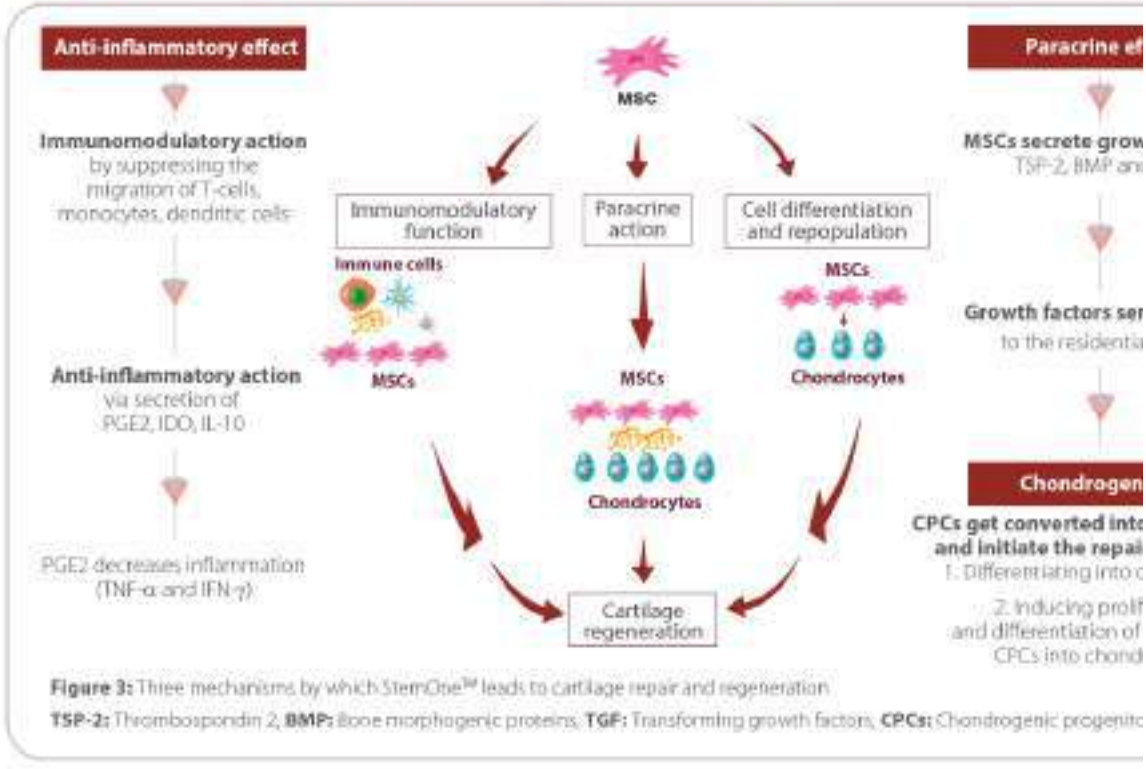

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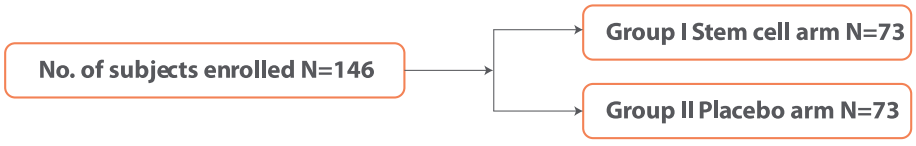
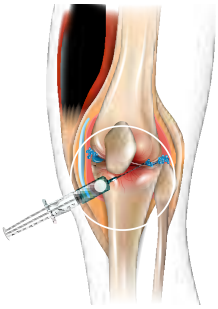
Randomized patient population in the study[2]



Efficacy[2]



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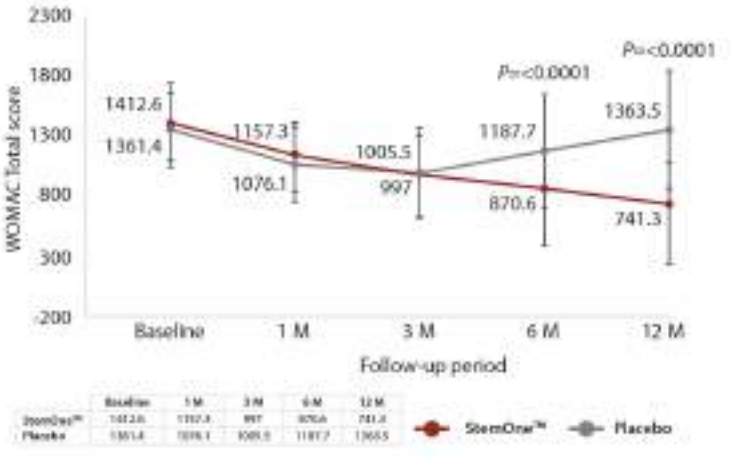
WOMAC
In a randomized, double-blind, multicentric, placebo-controlled, phase III study; the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) composite scores in terms of stiffness, physical function, and their composite in Grade II and III knee OA were found to be significantly lower in the StemOne™ arm compared to the placebo arm.



WOMAC (Total)
At 6 months follow up, the percentage of WOMAC - Total scores decreased by 23.64% in the StemOne™ arm as compared to the placebo arm, which further decreased to 45.60% at 1 year follow-up.

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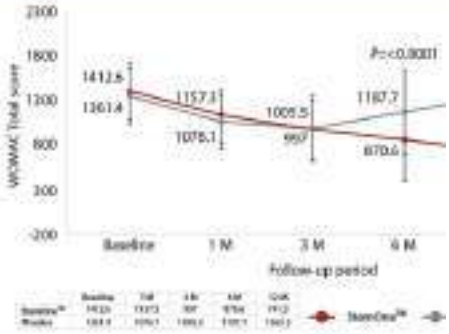

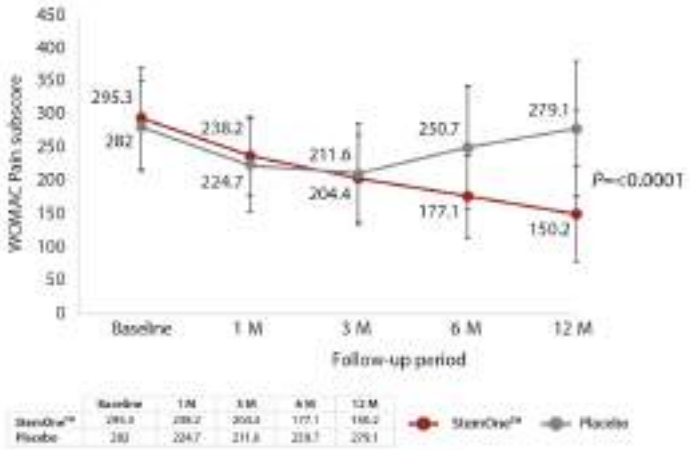

WOMAC (Pain)

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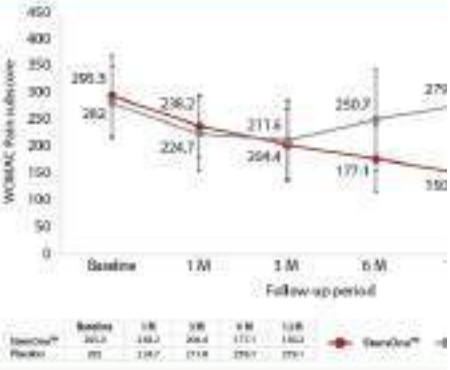

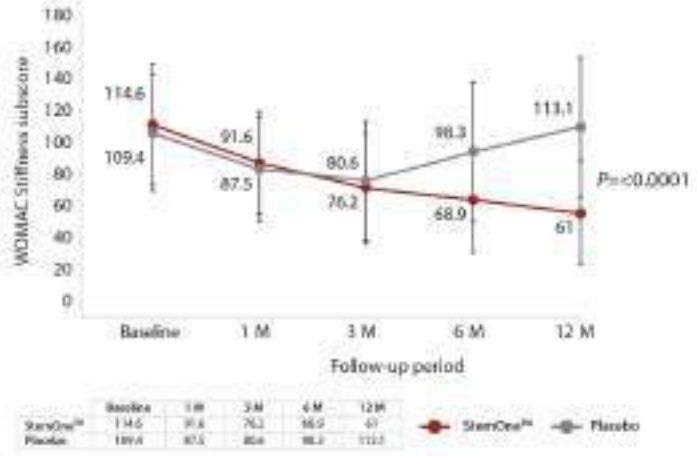

WOMAC (Stiffness)

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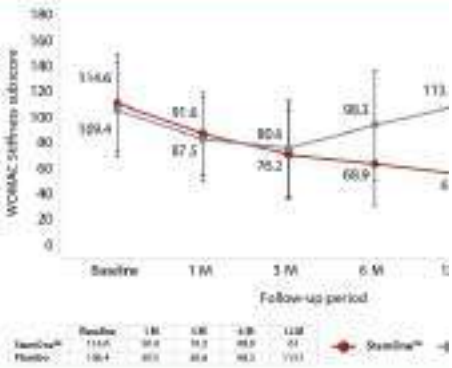

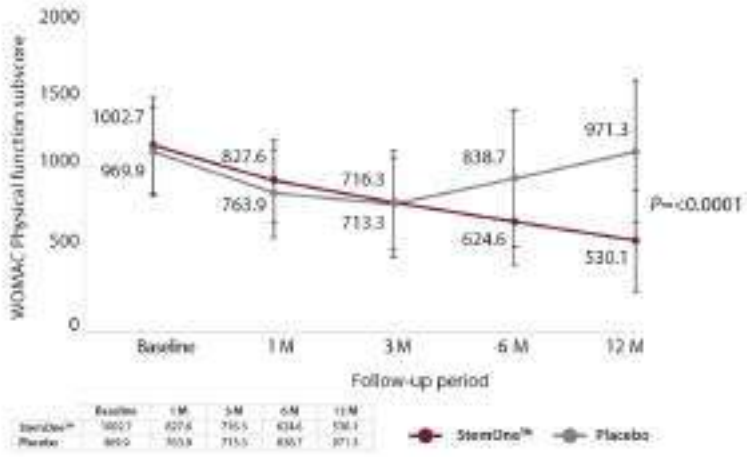

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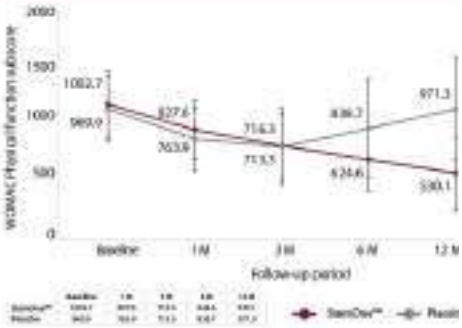
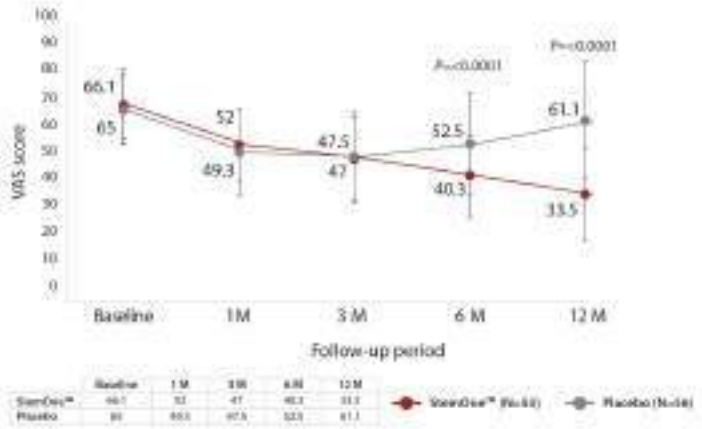


VAS



StemOne™ was found to be significantly superior to placebo in reducing pain, as is evident from the Visual Analog Scale (VAS) score changes.

At 6 months: Percentage of VAS score decreased by 39% in the StemOne™ arm as compared to the placebo arm, which was further decreased to 49.3% 1 year follow-up.

80.82% of patients had improvement ~20% in the StemOne™ arm at 1 year follow-up.

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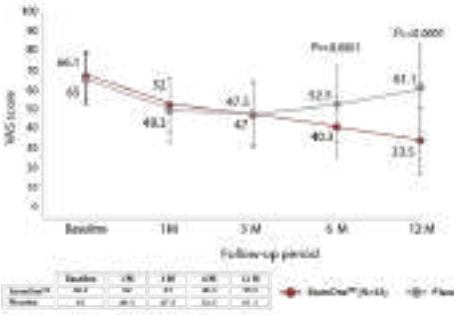


T2 Mapping[2]

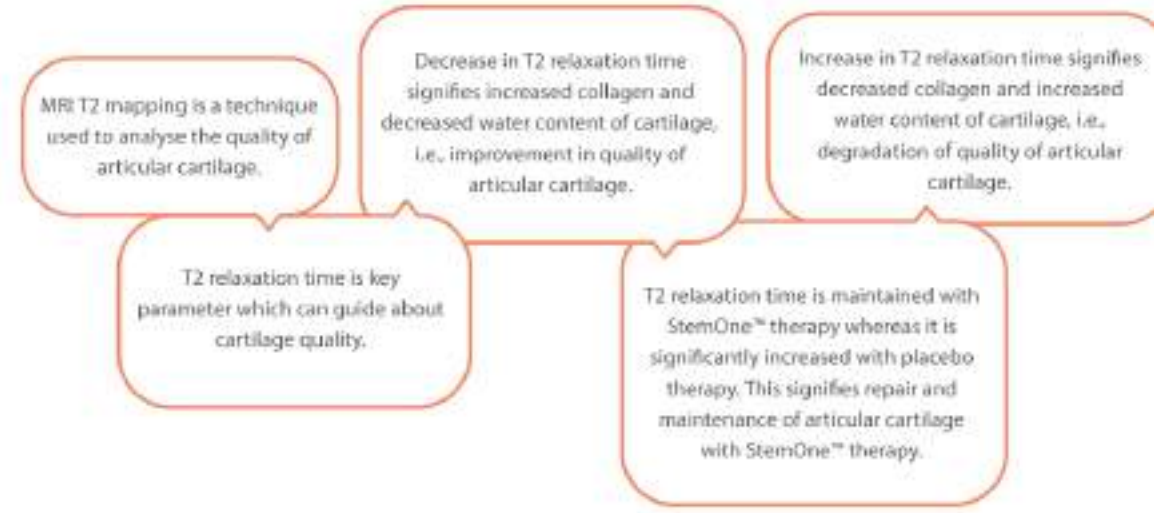
MRI T2 mapping is a technique used to analyse the quality of articular cartilage.

Decrease in T2 relaxation time signifies increased collagen and decreased water content of cartilage, i.e., improvement in quality of articular cartilage.

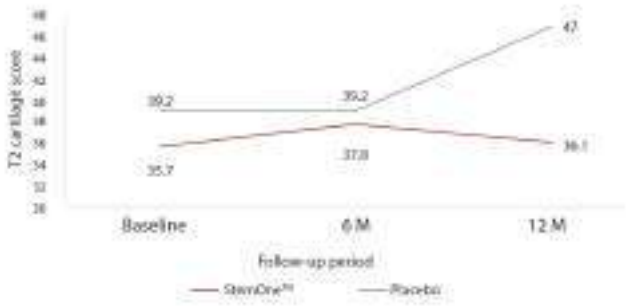
Increase in T2 relaxation time signifies decreased collagen and increased water content of cartilage, i.e., degradation of quality of articular cartilage.

T2 relaxation time is key parameter which can guide about cartilage quality.

T2 relaxation time is maintained with StemOne™ therapy whereas it is significantly increased with placebo therapy. This signifies repair and maintenance of articular cartilage with StemOne™ therapy.



Medial FT compartment - Deep cartilage (T2):



In the StemOne™ arm, the cartilage score was maintained compared to the placebo arm. There was a significant deterioration in the deep cartilage quality in the placebo group whereas the cartilage quality was maintained/improved in the StemOne™ group.

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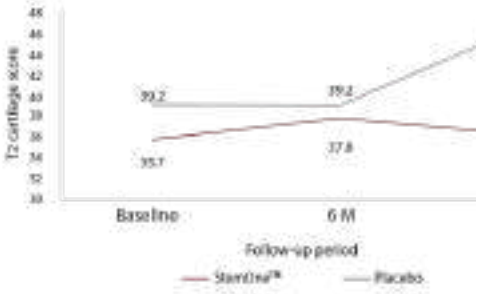

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a. StemOne™ arm

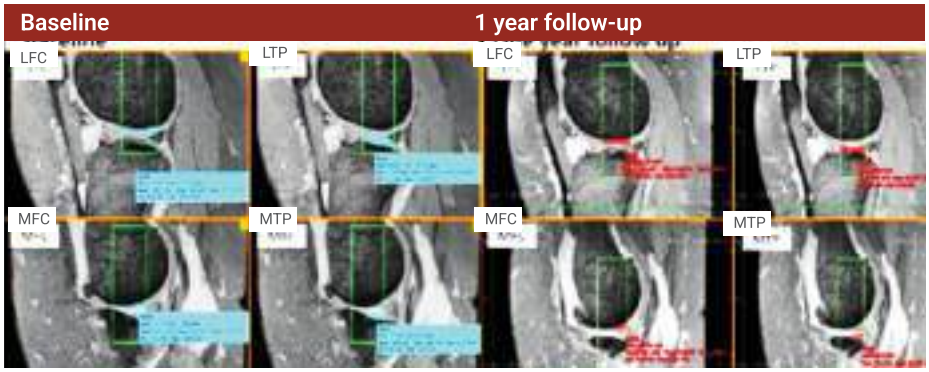
Medial femoral tibial (femoral) compartment - Deep cartilage T2 relaxation time decreased from 56.27 ms to 44.53 ms

b. Placebo arm

Increasing T2 values is associated with increase in water content and decrease in collagen content
Medial femoral tibial (femoral) compartment- Deep cartilage T2 relaxation time increased from 38.88 ms to 44.31 ms

Cartilage volume:

While only a modest increase in cartilage volume was observed in the placebo arm, a significant increase from approximately 521 to approximately 885 was witnessed in the StemOne™ arm.



Visit	MFC	MTP	LFC	LTP	Total
Baseline	56.93	128.09	193.76	142.135	520.915
Visit 7	153.07	122.725	301.67	307.48	884.945

StemOne™ arm: Significant increase in cartilage volume

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Baseline	56.93	128.09	193.76	142.135	520.915
Visit 7	153.07	122.725	301.67	307.48	884.945

Ideal Patient[2]

StemOne™ to be avoided in

1. Subchondral sclerosis involving both medial and lateral femorotibial compartments
2. Complete ACL/PCL tears
3. Grade 3 complete root tears of the meniscus

Packaging and shipping[2]

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A dry shipper (cryo-shipper) is an insulated cryogenic container that contains refrigerated liquid nitrogen absorbed into a porous lining. It is designed to safely transport a variety of materials at cryogenic temperatures. Storage temperature inside the shipping chamber remains at -185°C to 196°C until the liquid nitrogen evaporates from the absorbent material. Cell and gene therapies are regularly shipped in this specialized container.

This lid is lifted and the canister stand is carefully slid out of the cryo-shipper. The vial box is now securely placed into the canister stand. Once placed, the canister stand is securely returned to the cryo-shipper.

An integral temperature monitor which measures the inside temperature of the cryo-shipper is fixed to the lid.

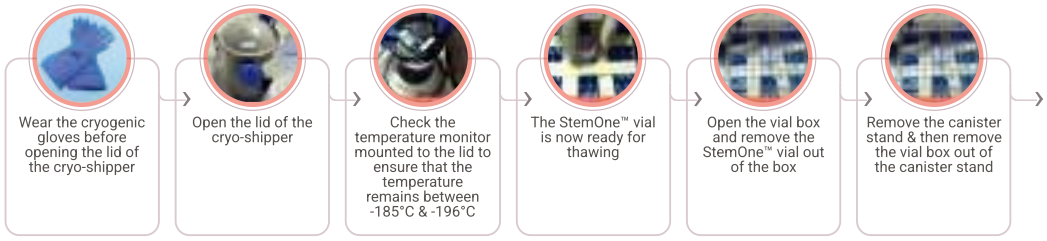
Patient preparation and administration[2]

1 The patient must be premedicated with IV injections of:[17]

100 mg Hydrocortisone (1 vial) + **45.5 mg** Pheniramine maleate (2 ml)

2 StemOne™ should be administered within 60 minutes of premedication[17]

Retrieval of the StemOne™ vial from the cryo-shipper[2]



Thawing and reconstitution[2]

StemOne™ vial immersed in pre-heated water bath (37±1°C) for 3 to 4 minutes

Aspirate 1 ml of Plasmalyte-A using 5 ml syringe and 18G needle

Flip open the seal of the vial

Inject the aspirated 1 ml Plasmalyte-A into the StemOne™ vial by inserting the 18G needle attached to the 5 ml syringe into the rubber stopper

Rubber stopper that is visible in the centre of the aluminium seal

Attach the given 5 ml syringe to the 18G needle, aspirate the entire suspension into the syringe

StemOne™ injection is ready for injecting followed by HA provided in the kit

StemOne™ administration[2]

The StemOne™ injection should be administered intra-articularly, using a 5 ml syringe, under all aseptic precautions.

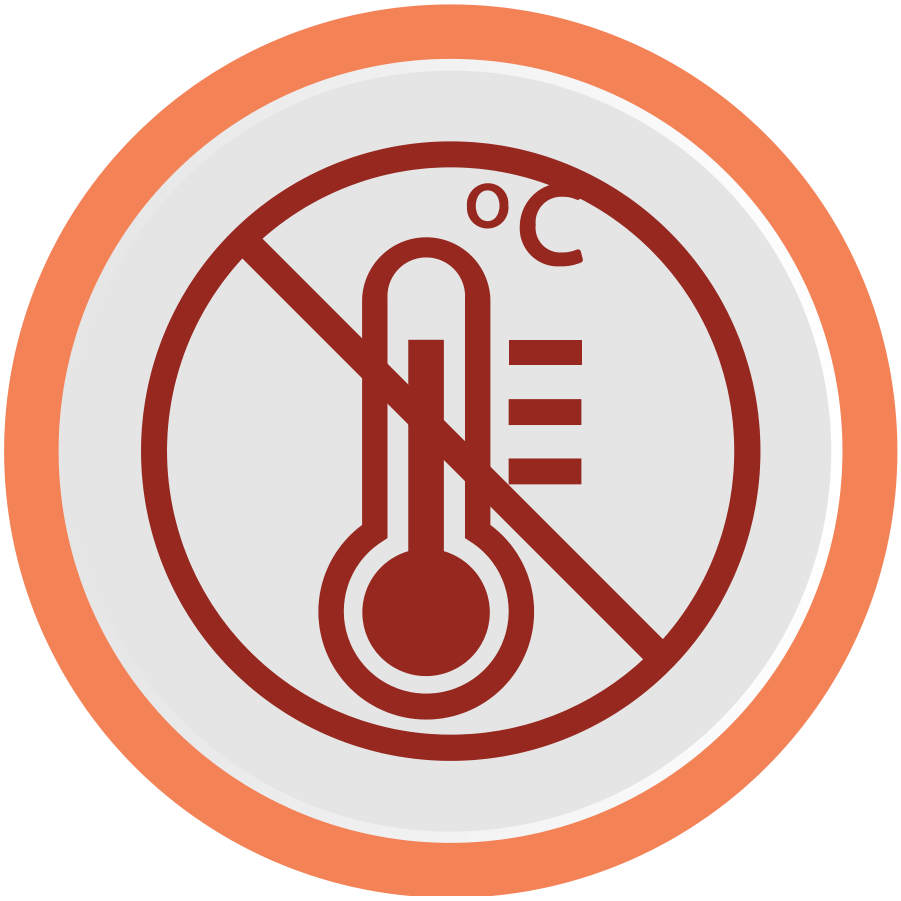
The StemOne™ injection should be injected immediately after preparation and should not be stored.

The intra-articular injection should be administered using a 2-inch (5.1 cm) 20G needle mostly as a medial or lateral parapatellar injection (an injection into the patellofemoral joint). However, optimal joint positioning and site of needle insertion for the affected knee may vary according to the anatomic and pathologic conditions present.

After injecting StemOne™, the syringe should be detached from the 20G needle (which is not removed from the site of injection) and HA (molecular weight 500,000 – 730,000 Daltons), which is a pre-filled syringe, should be injected through the same needle. Thus, piercing of the

needle intra-articularly will be done only once.

The StemOne™ injection should not be used if:



The temperature logger displays a temperature above −185°C, when the StemOne™ vial is being recovered from the cryo-shipper.

The StemOne™ vial is found to be damaged or leaking.

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Precautions[6]

0-3 Days post intra-articular injection	
Patients should rest for 24 hours after the injection except for bio breaks	Strenuous or prolonged weight-bearing activities must be avoided by the patients for 72 hours after the injection
Patients should stay hydrated, eat regular food & drink plenty of water to promote healing	Patients should not take any medications without your knowledge
Only cold packs may be applied, if required, by patients on the injection area	Patients should not apply hot packs over, or massage, the injection area
Patients may take bath with lukewarm water after 24 hours	Bathing with very hot water must be avoided by patients
	Patients should not smoke or drink alcohol
3-14 Days post intra-articular injection	
Patients should gradually increase their daily activities and exercise	Patients should avoid drinking alcoholic beverages in the first 7 days

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Note: NSAIDs can be used for manangement of pain

Merit of StemOne™ [2]

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References:

1. Loo SJQ, Wong NK. Advantages and challenges of stem cell therapy for osteoarthritis (Review). Biomed Rep. 2021;15:67.
2. Data on file.
3. Thej C, Gupta PK. The role of mesenchymal stromal cells in the management of osteoarthritis of the knee. In: Al-Anazi KA, editor. Update on mesenchymal and induced pluripotent stem cells. London: IntechOpen. 2020.
4. Zha K, Li X, Yang Z, Tian G, Sun Z, Sui X, et al. Heterogeneity of mesenchymal stem cells in cartilage regeneration: from characterization to application. npj Regen Med. 2021;6:14.
5. Zhang X, He J, Wang W. Progress in the use of mesenchymal stromal cells for osteoarthritis treatment. Cytotherapy. 2021;23:459–70.

6. Northeast Knee Joint Institute Platelet-Rich Plasma (Post-Procedure) Guidelines. Available from: https://nkjinstitute.com/wp-content/uploads/2019/03/PRP-Post-Procedure-Guidelines.pdf Accessed on 19 Sep 2022.