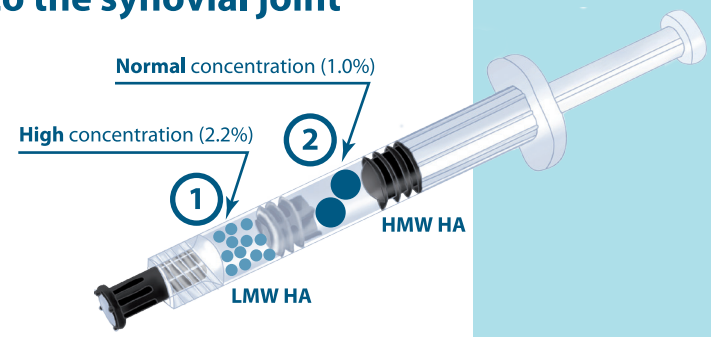
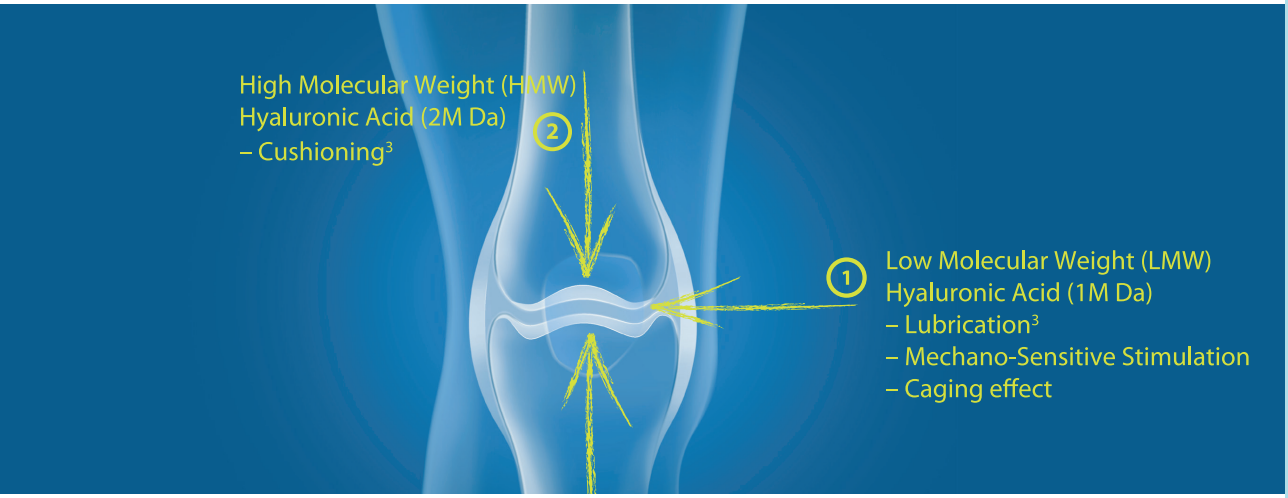
RenehaVis™

For the relief of pain and stiffness of the knee joint in patients with degenerative changes to the synovial joint

- **Dual molecular weight**
- **Dual concentration**
- **Dual action**





Mode of Action

- Both LMW and HMW HA are important for treating OA
- There are more functions for LMW HA compared to HMW HA
- The 3 functions of LMW HA are:
  1. Lubrication
  2. Mechano-Sensitive Stimulation – LMW HA accessing synoviocytes and stimulating it to produce more endogenous HA
  3. Caging effect – diffusing through cartilage to form proteoglycan complexes and protecting chondrocytes
- The function of HMW HA is:
  1. Shock absorption

Only RenehaVis™ provides Dual molecular weights of HA in 1 syringe

- ✓ **Clinically Proven with two years head to head comparison study: Strongest, fastest and longest symptom relief** [1]
- ✓ **Optimal therapeutic effects were achieved by two injections**[1]
- ✓ **Bio-synthetic** [2]
- ✓ **Optimal volume (1.4ml)**[1]

Pivotal 2 Year Study Parameters

- Blinded and randomised study with 4 arms and 200 patients
- Comparators used were:
  Placebo
  – Best available Low Molecular Weight (LMW) Hyaluronic Acid product
  – Best available High Molecular Weight (HMW) Hyaluronic Acid product
  – RenehaVis (Dual molecular weight (DMW) sodium hyaluronate)
- Assessment criteria used were pain (VAS) with walking, at rest, treatment satisfaction and reduction in concomitant analgesics
- Patients were assessed to 104 weeks (2 years) including retreatment if necessary at 52 weeks

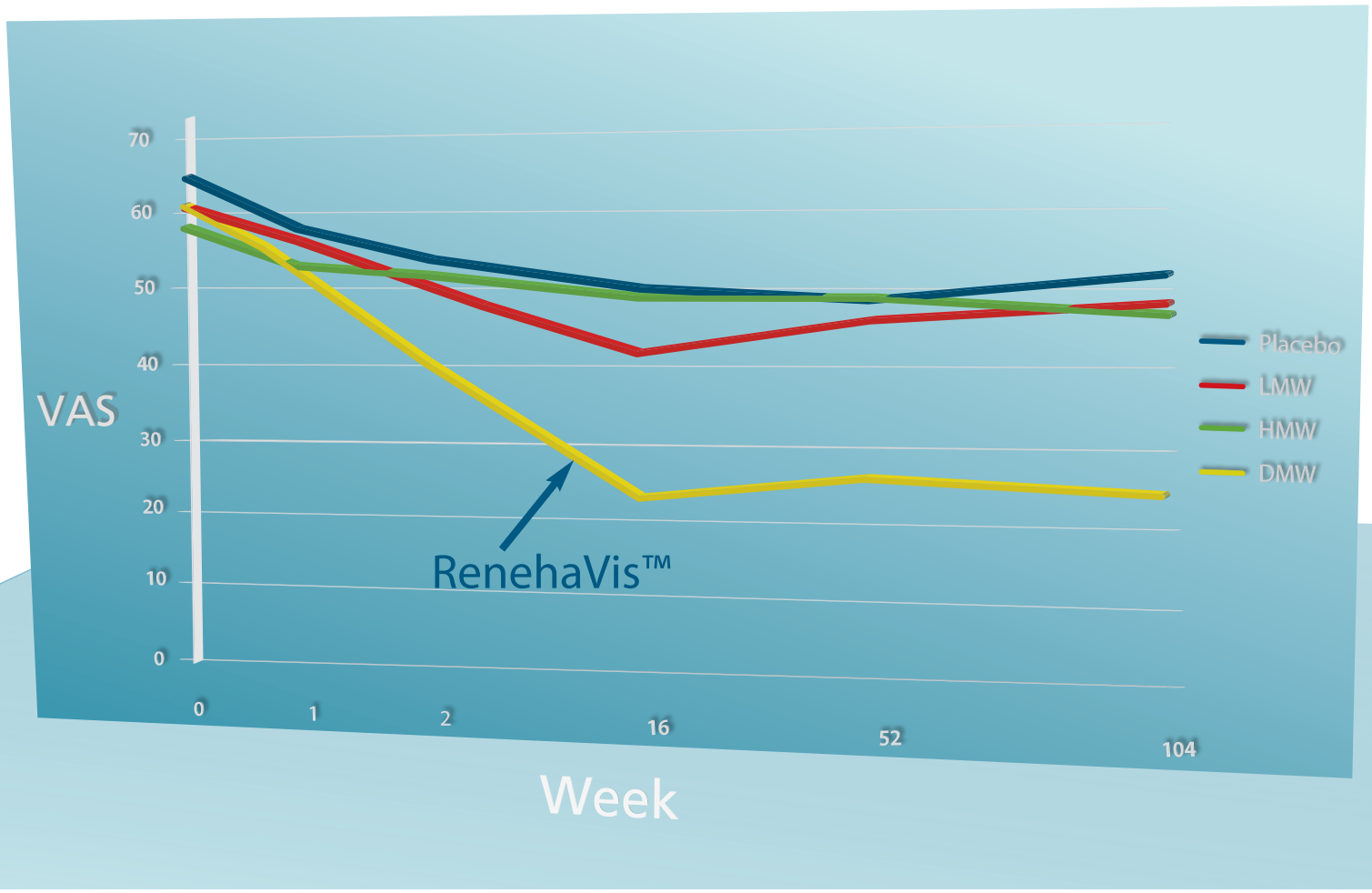
Key Conclusions

- RenehaVis (DMW) produced significantly faster, stronger and longer symptom relief compared to placebo, LMW and HMW both at rest and in activity
- Greatest symptom relief was maintained in the RenehaVis arm at all stages of the 2 year study
- Optimal therapeutic effects with RenehaVis were achieved by the 2nd injection suggesting that RenehaVis offers a short and easy treatment regimen of 1-3 injections depending on symptom severity
- Significantly higher level of patient satisfaction (88%) was achieved in the RenehaVis group compared to all other groups
- Significantly lower requirement of concomitant analgesics were required in the RenehaVis arm than the other treatment arms
- All patients re-treated at 52 weeks with RenehaVis experienced similar or even greater reduction in VAS compared to the first treatment
- RenehaVis was well tolerated and safe

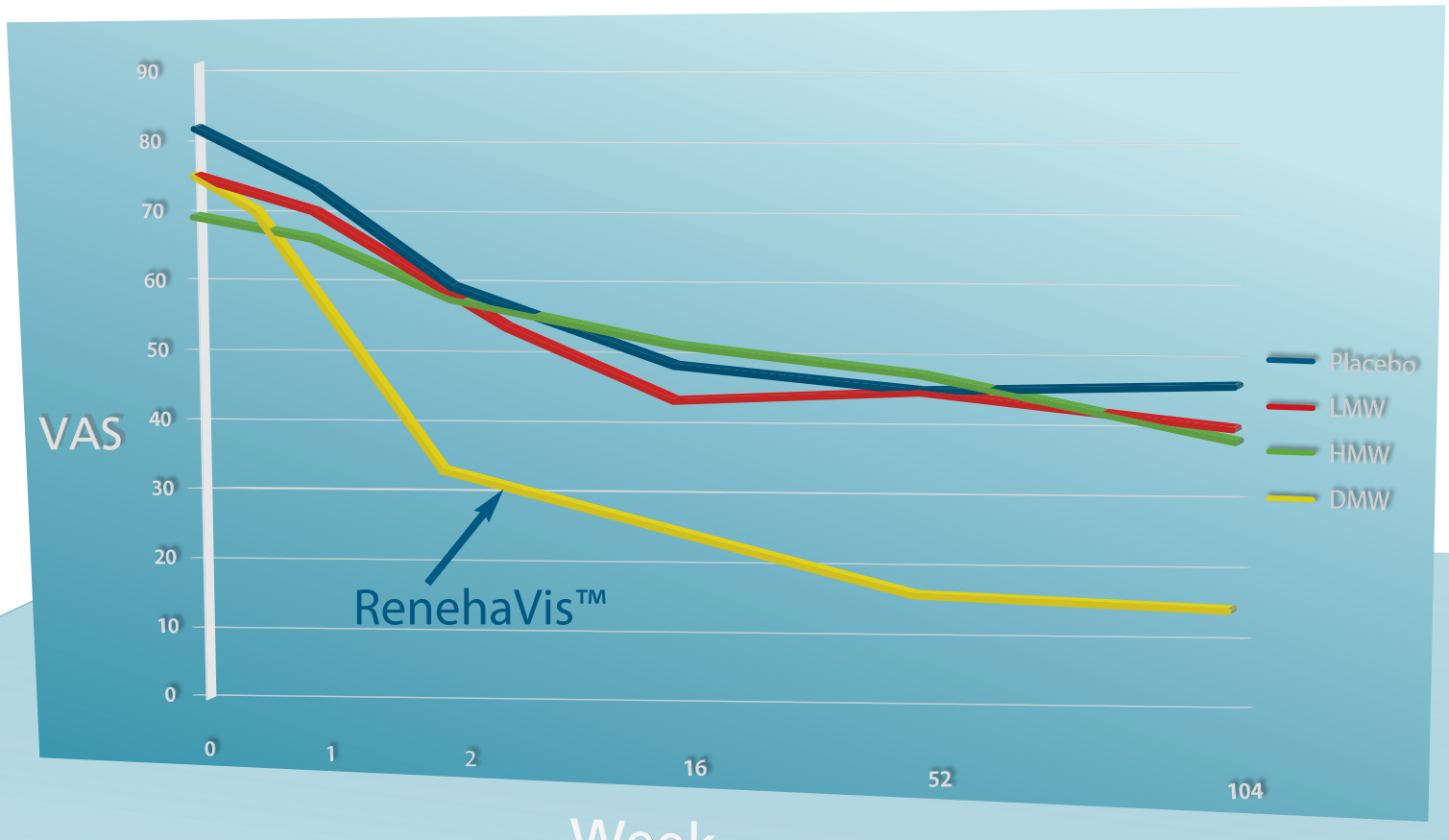
Reference:

1. Robert J. Petrella, Long terms efficacy and safety of a combined low and high molecular weight hyaluronic acid in the treatment of osteoarthritis of the knee. Rheumatology Reports 20101; volume 3:e4
2. RenehaVis Prescribing Information
3. Ghosh P, Guidolin D. Potential mechanism of action of intra-articular hyaluronan therapy in osteoarthritis: are the effects molecular-weight dependent? *Semin Arthritis Rheum.* 2002;32(1):10-37.

Resting VAS score



Walking VAS score



RenehaVis™

For knee dynamic needs

RenehaVis™ is two clear solutions of sterile sodium hyaluronate in a phosphate buffered saline contained in a two chamber pre-filled syringe for single intra-articular injection into the synovial space of the joint.

RenehaVis™ 0.7ml LMW and 0.7ml HMW, terminally sterilised by moist heat, is enclosed within a glass, ready to use, disposable syringe. The syringe is packed within a blister pack and an outer cardboard carton.

RenehaVis™ is a sterile pre-filled two-chamber glass ready to use disposable syringe containing:

Chamber 1 > Sodium hyaluronate **Low Molecular Weight (LMW)** 0.7ml sterile **2.2%** sodium hyaluronate **1 x 10⁶ Da** molecular weight.

Chamber 2 > Sodium hyaluronate **High Molecular Weight (HMW)** 0.7ml sterile **1.0%** sodium hyaluronate **2 x 10⁶ Da** molecular weight.

Dosage and Administration

Injection of **RenehaVis**™ should only be made by a Healthcare Professional trained in the technique.

The dosage regimen is injection into the affected synovial joint space once a week for up to three inejctions depending on the severity of the degenerative change to the knee joint.

Clean the skin around the injection site with antiseptic and allow to dry before injection is given.

If joint effusion is present it should be aspirated before injection of **RenehaVis**™.

Aspiration of a small amount of synovial fluid as part of the injection procedure to ensure the correct positioning of the needle is possible.

Before proceeding, ensure that the plunger rod is tightly screwed into the plunger stopper.

The contents of the syringe are sterile and should be injected using a sterile needle of an appropriate size (25 gauge needle is recommended). The syringe is fitted with a Luer lock (6%).

Discard the syringe and needle after single use.

Uses

For the relief of pain and stiffness of the knee joint in patients with degenerative changes to the synovial joint.

The duration of effect in patients with grade 1 to 3 medial compartment osteoarthritis has been demonstrated to be up to twelve months.

The performance of **RenehaVis**™ is due to its biocompatibility and physicochemical properties. The LMW and HMW sodium hyaluronate contained in **RenehaVis**™ is a biopolymer composed of repeating disaccharide units of N-acetylglucosamine and glucuronic acid and though it is biosynthesised by the bacterium *Streptococcus equi* it has been shown to be the same as the sodium hyaluronate which is found in the human body. **RenehaVis**™ supplements the endogenous Sodium Hyaluronate found naturally in the synovium but which has been depleted by degenerative and traumatic changes to the synovial joint.

Contra-indications

Patients with known sensitivity to sodium hyaluronate.

Warnings and Precautions

Do not inject **RenehaVis**™ if the area of the injection is infected or where there is evidence of skin disease.

RenehaVis™ pre-filled syringe is single use. The contents of the syringe should be used for one injection only. Any remaining sodium hyaluronate should be discarded. If a syringe is retained for a subsequent injection there is a risk of contamination resulting in the possible infection of the patient and/or foreign body reaction.

RenehaVis™ should not be re-sterilised as the device performance may be compromised which could cause serious harm to the patient's health and safety.

Sodium hyaluronate is manufactured by fermentation of *Streptococcus equi* and rigorously purified. However, the physician should consider the immunological and potential risks that can be associated with the injection of any biological material.

Do not use for children.

There is no evidence concerning the safety of **RenehaVis**™ in human pregnancy and lactation. Administration during pregnancy and lactation is at the discretion of the orthopaedic surgeon.

Do not use if sterile packaging has been damaged.

Do not use after the expiry date.

Follow national or local guidelines for the safe use and disposal of needles. Obtain prompt medical attention if injury occurs.

Adverse Reactions

Transient pain and swelling may occur with intra-articular injections.

Transient increases in inflammation in the injected synovial joint following injection of **RenehaVis**™ may occur in patients with inflammatory osteoarthritis.

Rarely an inflammatory reaction could occur which may or may not be associated with **RenehaVis**™.

Incompatibilities

RenehaVis™ has not been tested for compatibility with other substances for intra-articular injection. Therefore the mixing or simultaneous administration with other intra-articular injectables is not recommended.

Storage

Store between 2°C and 25°C. Do not freeze. Protect from light.

Do not use if sterile packaging has been damaged.

Do not use after expiry date.

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