Significant reduction of the Serum Levels of a Specific Biomarker of Cartilage Degradation (Coll2-1) following Viscosupplementation Compared to saline solution in patients with Knee Osteoarthritis: the EPIKART Study

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The EPIKART study

- A 6-month prospective, randomized, double blind, controlled study
- A single injection of KARTILAGE®Cross or saline solution

**KARTILAGE®Cross**
- 2.2 ml (16 mg HA/ml)
- Reticulated
- Biofermentation
- Mannitol (35 mg/g of gel)
Inclusion criteria

- Men or women aged between 45 and 80 years old
- With symptomatic femoro-tibial OA (ACR criteria)
- Lack of efficacy of NSAIDS or Paracetamol
- Mean global pain during the last 24 h VAS > 40 mm
- K&L II or III
Primary outcome:
The variation of Coll2-1 in serum between inclusion visit (D-10) and D90 (3 months after injection) expressed as the % of patients with a Coll2-1 variation over 10 nmol/l (Δ D-10 – D90)

Secondary outcomes:
- Lequesne Index and pain (VAS) variation
- NSAIDS and paracetamol consumption
- Global patient assessment
- OARSI-OMERACT responders
- Other biomarkers variation: Coll2-1NO2, myeloperoxidase, usCRP
Coll2-1 and Coll2-1NO2: two cartilage specific biomarkers

- Specific of degraded cartilage
- Measure cartilage catabolism
EPIKART: Study design

- Lequesne Index Global patient assessment
- Safety

Kartilage® Cross

- D-10
- D30
- D90
- D180

sColl2-1, sColl2-1NO2, MPO, usCRP

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Flow Chart

Selected Patients 84

Randomized patients 81 patients

- Saline solution
  40 patients
  ITT/FAS/safety
  PP
  35 patients

- Kartilage®Cross
  41 patients
  ITT/FAS/safety
  PP
  31 patients
Population

Characteristics of the FAS population (N=81)

<table>
<thead>
<tr>
<th></th>
<th>Kartilage®Cross N=40</th>
<th>Saline solution N=41</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.9 ± 10.4</td>
<td>63.0 ± 8.9</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>- Women</td>
<td>62.5 %</td>
<td>75.6 %</td>
<td>0.20</td>
</tr>
<tr>
<td>- Men</td>
<td>37.5 %</td>
<td>24.4 %</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.0 ± 7.4</td>
<td>30.8 ± 7.2</td>
<td>0.24</td>
</tr>
<tr>
<td>History (years)</td>
<td>7.6 ± 8</td>
<td>5.9 ± 5.3</td>
<td>0.26</td>
</tr>
<tr>
<td>Pain intensity</td>
<td>65.7 ±11.6</td>
<td>66.4 ±10.6</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Kartilage®Cross decreased Coll2-1 in the FAS population

<table>
<thead>
<tr>
<th></th>
<th>Kartilage®Cross N=40 at D-10</th>
<th>Saline solution N=41 at D-10</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Coll2-1 at D-10</td>
<td>840.3 ± 375.8 (N=40)</td>
<td>766.1 ± 359.2 (N=41)</td>
<td>0.3663</td>
</tr>
<tr>
<td>Serum Coll2-1 at D90</td>
<td>745.4 ± 343.5 (N=37)</td>
<td>782.3 ± 233.7 (N=35)</td>
<td>0.5975</td>
</tr>
<tr>
<td>Adjustment on basal value</td>
<td>-80.2 ± 44.1</td>
<td>-14.6 ± 45.3</td>
<td>0.0030</td>
</tr>
<tr>
<td>Reduction of at least 10 nmol/l</td>
<td>56.8 %</td>
<td>28.6 %</td>
<td>0.0158</td>
</tr>
</tbody>
</table>
Coll2-1 variation with time

![Graph showing the variation of Coll2-1 with time (days) for Kartilage Cross and Saline solution. The graph indicates a decrease in serum Coll2-1 (%) for Kartilage Cross and an increase for Saline solution over time.]
Secondary Outcomes

- No significant effect on Pain intensity
- No significant effect on Lesquesne index
- No significant change in OMERACT-OARSI responders
- No significant modification of other biomarkers
Conclusions

- KARTILAGE®Cross induced a significant reduction of cartilage catabolism 90 days after treatment.
  → Mechanical effect?
  → Biological activity?

- Coll2-1 is a useful tool for objectively evaluate viscosupplementation effect
  → sensitive to metabolic change occurring in a single joint.
Thank you for your attention!

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