LIPOGEMS
Your cells for your health

Lipogems in Osteoarthritis

January 2020

- **Lipogems in Osteoarthritis**

- **Clinical Data and Trials**
  - Knee
  - Other (Shoulder, Hip)
  - Clinical Trials and Publications

Osteoarthritis

- Osteoarthritis (OA) is a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro- inflammatory pathways of innate immunity.

- There is a lot of current evidence in the literature that suggests anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness.

- The illness is characterized by joint pain, swelling and stiffness that leads to activity limitations, participation restrictions, sleep interruption, fatigue and depressed or anxious mood, and ultimately loss of independence and reduced quality of life.

- OA has a significant impact on day-to-day functioning and, although the levels of pain and disability may fluctuate, it has no known cure or spontaneous remission and is associated with irreversible structural damage and progression over time.

Source: OARSI

Osteoarthritis – A global epidemic

- **Osteoarthritis** affects approximately **250 million people** globally (3.6% of the population) and causes moderate to severe **disability in 43.4 million** people.

- Osteoarthritis (OA) affects an estimated **31m Americans**:
  - Leading Cause of Disability in American Adults
  - **Prevalence Increases with Age**
    - 80% Incidence in Persons Over 75
  - 14m Americans Suffer Symptomatic Knee OA
  - Ca. 3.5m Americans expected to undergo knee replacement and 0.5m hip replacement yearly by 2030

- **Huge economic burden** to society
  - In 2003 the total costs attributable to arthritis and other rheumatic conditions (AORC) in the US was approximately USD128 billion equalling 1.2% of the 2003 US gross domestic product.
    - Direct costs totalled $80.8 billion (i.e., medical expenditures) and indirect costs were USD47.0 billion (i.e., lost earnings).
  - A US study in 2009 estimated costs due to hospital expenditures of total knee and hip joint replacements to be USD28.5 billion and USD13.7 billion respectively.

Source: OARSI, Arthritis Foundation, MiMedx, Lipogems

Osteoarthritis – Unmet Medical Need

- **Multiple treatments, no cure**
  - Numerous **non-pharmacologic and pharmacologic interventions** for OA
    - Integrated models of patient focused multi-disciplinary care have been shown to reduce pain, improve function and quality of life
  - Available medications that promise to mitigate the pain of OA have **significant safety risk**.

    > Non-steroidal anti-inflammatory drugs (NSAIDs) have been associated with a clinically relevant (as high as 50 to 100%) increase in the risk of myocardial infarction or cardiovascular death compared with placebo [CNT Collaboration].

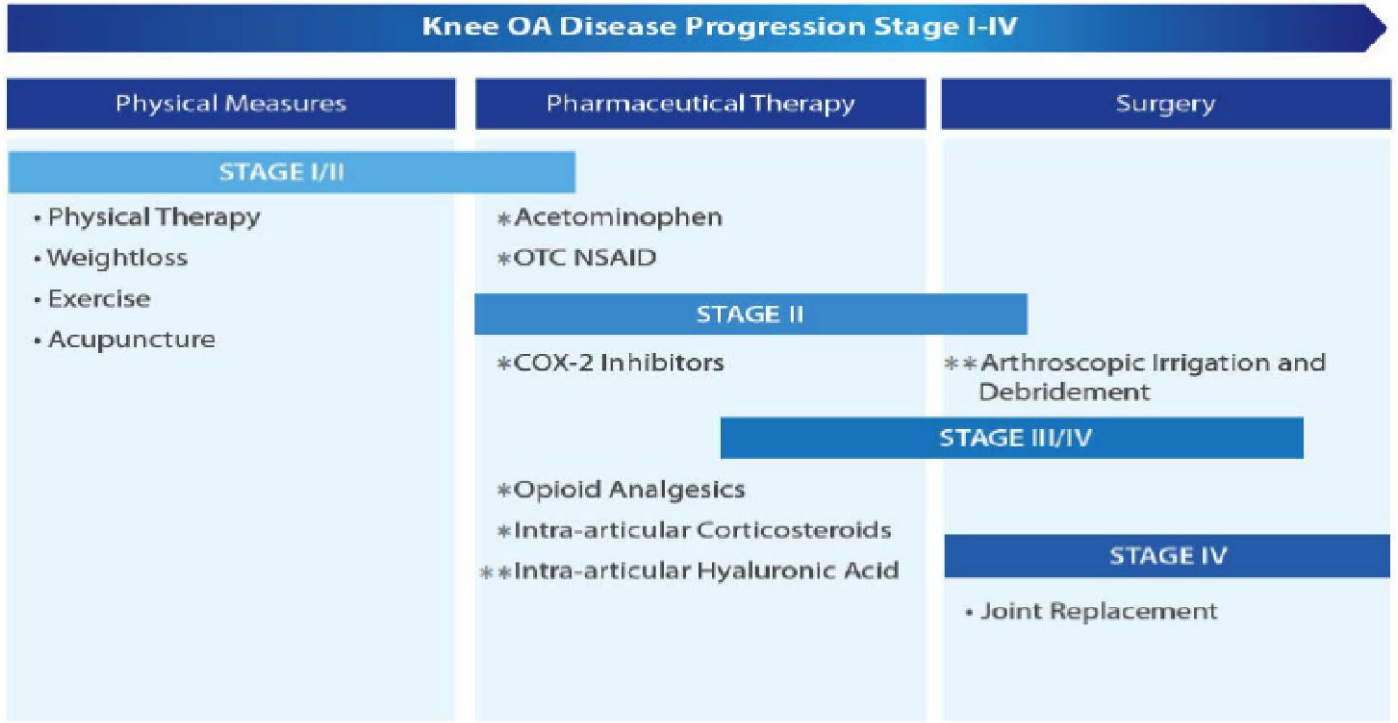
  - **No approved disease modifying option**. Presently there are no drugs approved that can prevent, stop, or even restrain progression of OA.

- **Total hip or knee joint replacement is the end result for millions of OA patients worldwide.**
  - Actual rate of total joint replacement may significantly underestimate the true need
    - Personal and system factors are barriers to appropriate care
  - Joint replacement does not equate with remission or reversal of disability, but rather lessens disease severity in the replaced joint; it does not solve the problem.
    - Most people continue to suffer some physical impairment following joint replacement
    - As many as 20-30% continue to experience pain and disability after total joint replacements
    - One in five require joint replacement in another joint within two years.

Source: OARSI

Osteoarthritis: Treatment Options

- **Steroids**:
  - Evidence
    - Anti-inflammatory action for Synovitis
    - Diminished early inflammatory response
    - Tissue atrophy and degeneration
  - Indication
    - **Acute treatment** (active Synovitis or Effusions)
    - Not for chronicle treatment
- **Viscosupplementation** (Hyaluronic Acid)
  - Evidence
    - Contradictory results from published clinical data (Placebo)
    - Efficacy in pain reduction at 3/6 months, but comparable to placebo or physiotherapy
  - Indication
    - General indication in OA
- **PRP:**
  - Evidence:
    - Superior efficacy than HA/Steroids at 6 months
    - Doubtful results after 12 months and with higher grade OA



*Toxic side effects, ** Limited efficacy.
Source: Arthritis Foundation, MiMedx, Lipogems

Strong need for a non-surgical disease-modifying solution across the whole OA spectrum

Lipogems and Osteoarthritis (1/2)

- In excess of 40.000 Lipogems procedures completed on OA human patients with no major related adverse effect recorded. No sign of chondro-toxicity.
  - Knee and other joints

- Results point to Lipogems injection as viable approach for the management of diffuse degenerative knee chondropathy in the long-term (up to three years data available).

- Scientists suggest that Lipogems, via trophic and immunomodulatory mechanisms, induces host chondrocytes to produce an extracellular matrix that consequently influences structural and biochemical changes in the cartilage*.

*Hudetz et al.

- OA Stage II- III – IV (KL Scale)

Kellgren-Lawrence (KL) grading scale for OA:

Grade 0	normal
Grade 1	doubtful joint space narrowing (JSN) and possible osteophytic lipping
Grade 2	definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph multiple osteophytes, definite JSN, sclerosis, possible bony deformity
Grade 3	multiple osteophytes, definite JSN, sclerosis, possible bony deformity
Grade 4	large osteophytes, marked JSN, severe sclerosis and definite bony deformity

Lipogems and Osteoarthritis (2/2)

- **Multiple investigator-initiated published Clinical studies** in Europe and the USA.
  - Main Focus on Knee Osteoarthritis
  - Disease Stage:
    - **Mild/Medium** OA (KL (II to III)
    - **Severe** OA (KL III to IV),
  - Procedure Type:
    - **Standalone Injection**
    - **Injection during Surgery** (Arthroscopy)
- **Priority targets**:
  - KL III/IV, "**Ready for metal**", over 60 y.o., (approx. 4m patients)
  - "**Treatment Gap**" patients (severe OA non eligible/non ready for Arthroplasty or seeking alternatives): est. 2m in the USA

Procedure Type

- Standalone Intra-articular Infiltration
  - OA Stage II- IV
  - ***Disease Management/Joint Replacement postponement***
    - 6 clinical studies data reported in the following slides
- Injection during Surgery (Arthroscopy)
  - OA Stage III-IV
    - ***Joint replacement postponement***
      - 6 clinical studies data reported in the following slides

- **Lipogems-based procedures as a new potential candidate first/second-line treatment for mild to severe Knee Osteoarthritis**

- **Lipogems in Osteoarthritis**

- **Clinical Data and Trials**
  - **Knee**
  - Other (Shoulder, Hip)
  - Clinical Trials and Publications

Standalone Inj. – RCT Lipogems vs Steroids vs Placebo in Knee OA (Interim)

Study Purpose and Design:

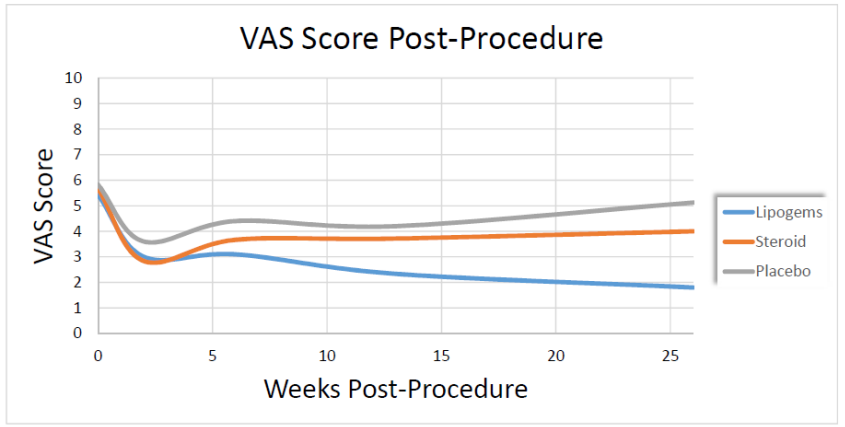
- Knee OA (VAS Pain score ≥ 3 (out of 10); KL 1-4
- MFat, intra-articular injection
- Level 1 RCT, MFat vs Corticosteroids vs Placebo (saline)
- 84 patients (28/28/28)
- University of New Mexico

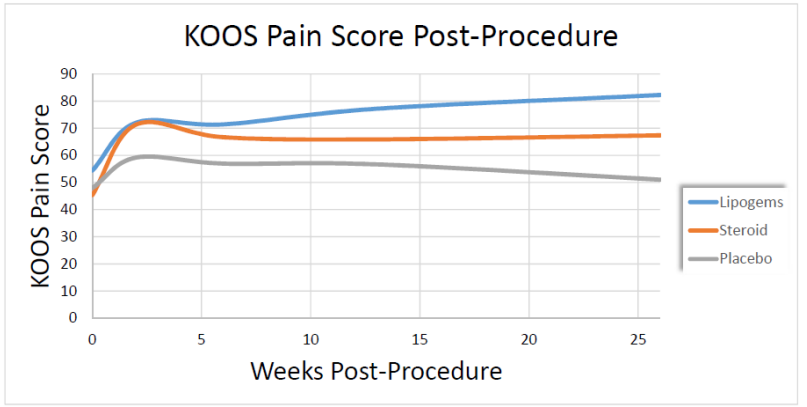
Endpoints:

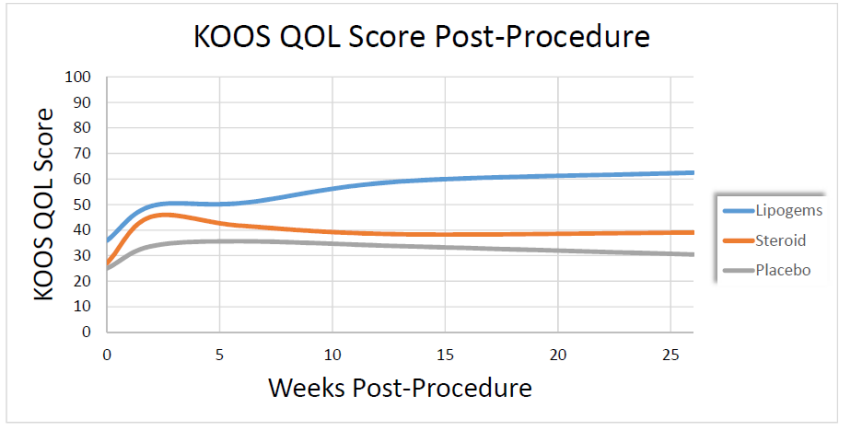
- **Safety:** type and incidence of any adverse event
- **Efficacy:** Complete VAS, WOMAC, and KOOS at 5 follow-up time points over a one year period

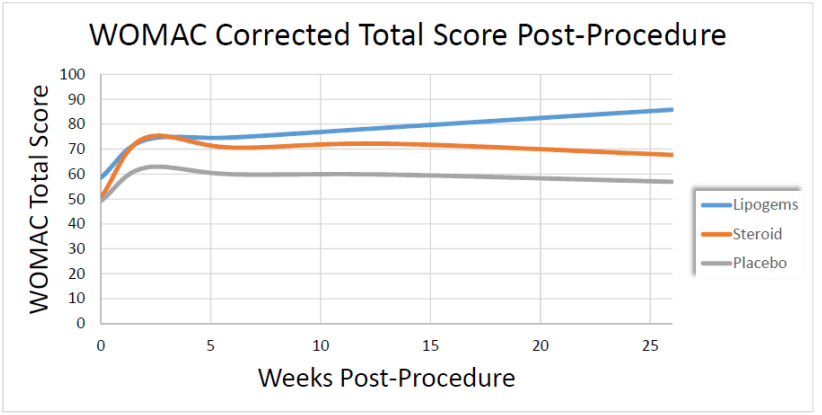
Results evaluation (interim data):

- **34 patients at 6 month follow-up post-injection**
  - 11 MFat
  - 12 Corticosteroid
  - 11 Saline placebo
- **Safety**: no adverse events,
- **Efficacy**:
  - MFat demonstrated significant improvements in all outcome measures at all time points examined









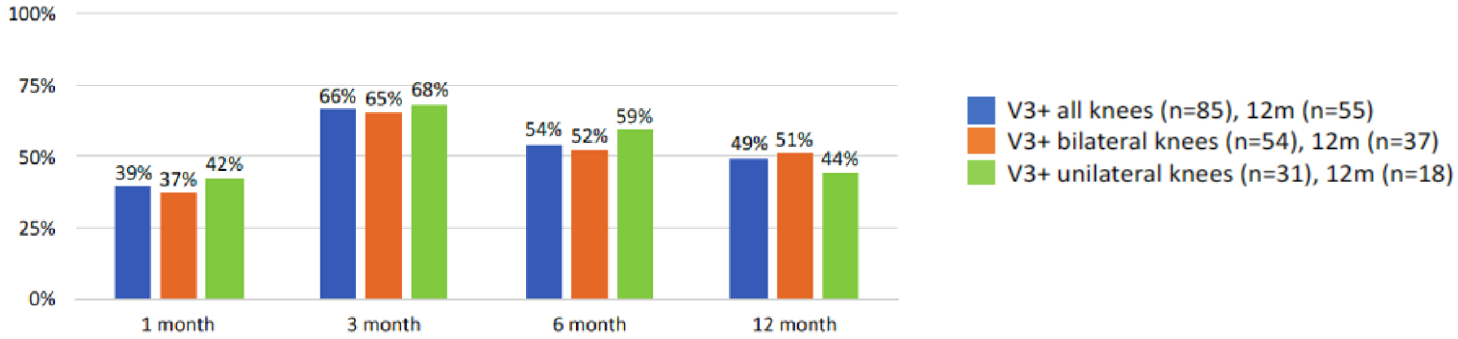
[1]Richter, Advances in Regenerative Medicine Conference, Vail 2019

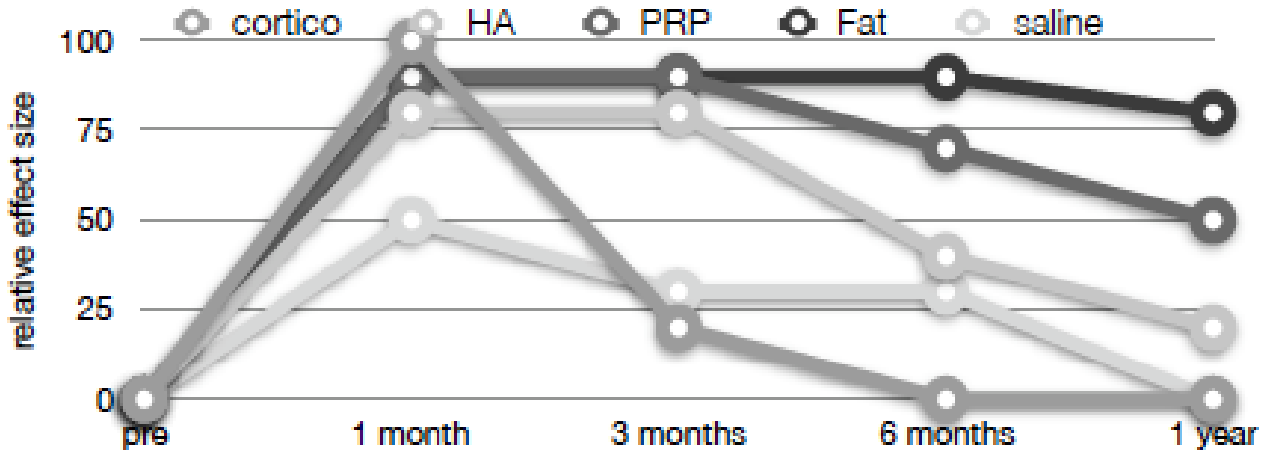
Standalone Inj. – Comparative Study in Knee OA

Study Design:
- Diffuse knee osteoarthritis
- MFat intra-articular injection
- Observational study, 58 patients enrolled (85 knees), 12 months follow-up
- Antwerp Orthopaedic Center, Monica Hospitals, (Antwerp, Belgium).

Endpoints:
- **Safety:** type and incidence of any adverse event during the study
- **Efficacy:** KOOS, and VAS pain scales at T0, 1, 3, 6, 12 months
  - 10 points of improvement in the scores considered clinically significant

Results evaluation :
- **Safety**: no adverse events,
- **Efficacy**:
  - % of responders in subgroups:
    - Prognosticators
      - Limited or absence of patellar synovitis 83%
      - Limited Bone Marrow Oedema 75%
    - OA grade:
      - High grade patella-femoral OA 50%
      - Moderate medial OA 70%
    - Gender
      - No difference
    - Meniscal tears:
      - No difference in outcome , but tendency to deteriorate earlier

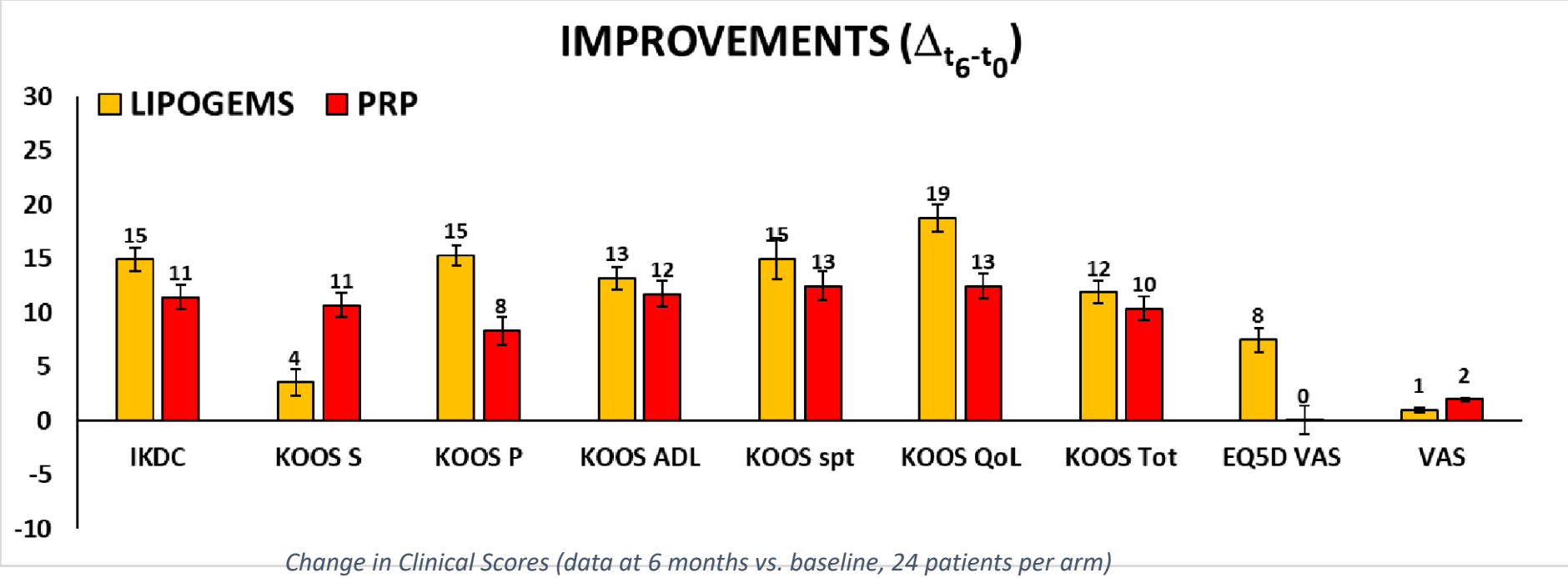




- Symptomatic improvement for all molecules: saline (up to 6 months) cortico (6 weeks), HA (6 months), PRP (1 year), Lipogems (longer)

[1]P. Verdonk, 5th International Knee Update, Davos (CH)

Standalone Inj. – Prospective RCT vs PRP in Knee OA (interim data)



Change in Clinical Scores (data at 6 months vs. baseline, 24 patients per arm)

Study Design:

- Knee osteoarthritis (grade II, III and IV)
- LIPOGEMS, single intra-articular injection
- Prospective Randomised study of 118 patients (control 1:1)
- Control: single injection of PRP
- Istituto Ortopedico Rizzoli (Bologna, Italy)

Endpoints:

- **Primary:**
  - **Efficacy at 6 months** by evaluation of KOOS, IKDC-subjective
- **Secondary:**
  - **Long term efficacy:**
    - 12 and 24 months KOOS, IKDC-subjective, Tegner Lysholm Knee and EQVAS
    - Objective joint tissue improvement by NMR and MOCART score
  - **Safety**: adverse events recording

[1]*Zaffagnini et al. SIGASCOT meeting, October 2018*

Standalone Inj. – Retrospective study Lipogems vs BMAC in Knee OA[1]

Study Purpose:

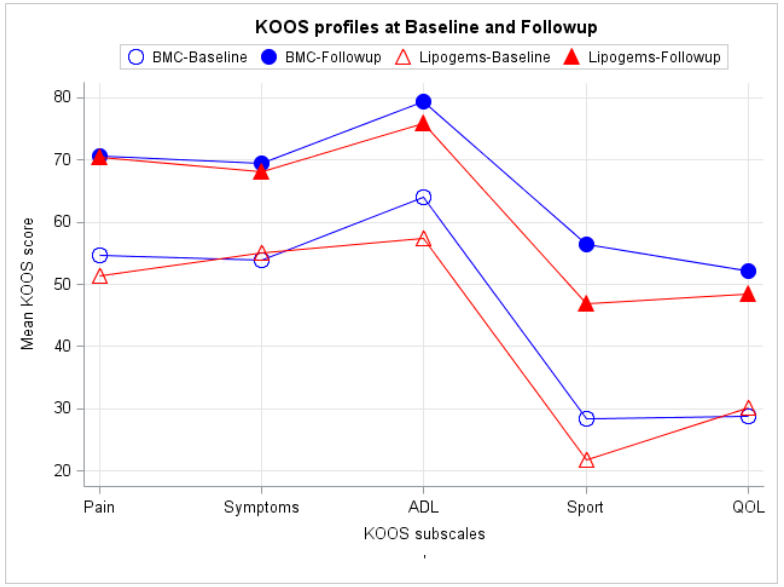
- Does MSC source (Adipose vs BM) affect outcomes?
- To determine pain and Patient Reported Outcomes (PRO's) in patients with symptomatic knee OA who received MFAT or bone marrow aspirate concentrate (BMAC) injection under ultrasound guidance.
- Retrospective study, 110 patients, Kellgren Lawrence scale range: I-IV.

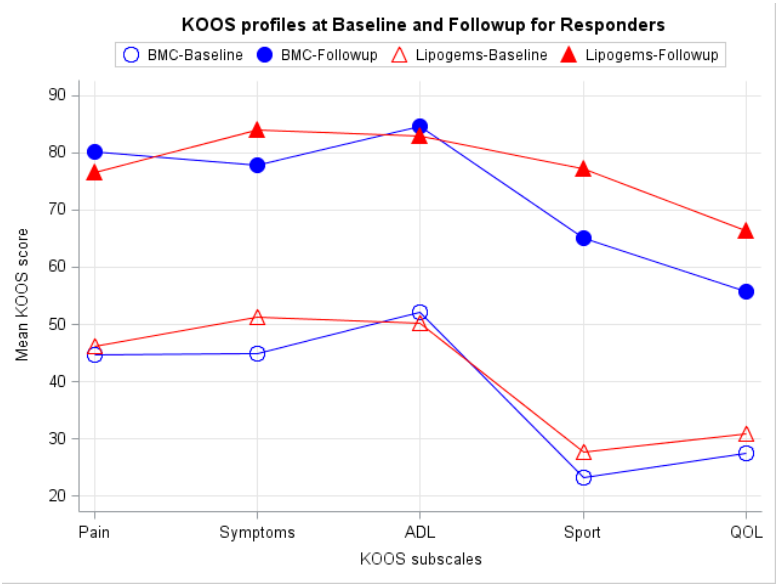
Endpoints:

- Prospectively follow all patients with BMAC or MFAT injection for symptomatic knee OA
- Surveys include KOOS, Emory Quality of Life (E-QOL) and VAS questionnaires
- Data compared to baseline in all patients and between BMAC and MFAT groups
- Follow up time points varied for each group

Results:

- Significant improvement in pain and function with MFAT or BMAC injection without a significant difference between treatment modalities
- Combined responders (at least 25% VAS reduction from baseline to follow-up): KL 1: 100%, KL 2: 73.9%, KL 3: 47.2%, KL 4: 55.6%





Temporal trends of scores for WOMAC, KOOD, EQ-5D and VAS in experimental group (blue line) and control group (red line)

- Equivalence to BMAC
- Broad inclusion criteria across the spectrum KL I-IV

[1]"Functional Outcomes Following Micro-Fragmented Adipose Tissue (MFAT) versus Bone Marrow Aspirate Concentrate (BMAC) Injections for Symptomatic Knee Osteoarthritis" Mautner and Bowers, Presented at AMSSM, 2018, Submitted for publication

Standalone Inj. – Pilot study in Severe Knee OA with 24 months F.u. (1/3)[1,2,3]

Study Design:

- A prospective, non-randomized, interventional, single-center, open label clinical trial of a single intra-articular injection of MFAT tissue,
- 17 patients enrolled, 32 knees assessed at 12 months. 10 patients/18 knees at 24 months (3 patients lost to TKA)
- Kellgren-Lawrence grade: III/IV
- St. Catherine Specialty Hospital, Zabok/Zagreb, Croatia

Endpoints:

- **Safety:** type and incidence of any adverse event during 24 months
- **Efficacy:** efficacy at 3, 6, 12, 24 months as assessed by radiological assessment (X-rays, MRI, dGEMRIC), biochemical laboratory test results, and clinical (VAS scale, WOMAC, KOOS scales)

Results evaluation :

- **Safety**: No adverse events recorded, no sign of chondrotoxicity
- **Efficacy:**
  - All clinical scales scale significantly improved at all measurements.
  - Increased Glycosaminoglycan (GAG) content in hyaline cartilage (as measured by dGEMRIC) versus the tendency to decrease with the course of OA.
  - GAG content correlates with quality of the cartilage extracellular matrix and its physical properties.

[1]Hudetz et al, Genes 2017, 8, 270,
[2]Boric et al, Genes 2019, 10, 1051
[2]Hudetz et al, 11th ISABS conf. 2019

Standalone Inj. – Pilot study in Severe Knee OA with 24 months FU (2/3)[1,2,3]

	Initial (M0)	First Follow-up (M3)	Second Follow-up (M6)	Third Follow-up (M12)	p * (M0–M3)	p * (M0–M6)	p * (M0–M12)
Visual analogue scale pain rating, resting; mean ± SD (min-max)	3.94 ± 2.56 (0–8)	1.24 ± 1.48 (0–4)	1.17 ± 1.62 (0–5)	0.56 ± 1.2 (0–4)	0.001	<0.001	<0.001
Visual analogue scale pain rating, movement; mean ± SD (min-max)	7.33 ± 1.72 (4–10)	3.82 ± 2.07 (1–7)	3.67 ± 2.03 (0–7)	3.17 ± 1.98 (0–7)	<0.001	<0.001	<0.001

* *Pair-wise testing with t-test for paired samples*; SD: standard deviation; M: months

Fourth Follow-up (M24):
- resting VAS had decreased from 4.45 2.42 to 0.55 1.04 (p < 0.001),
- activity VAS had decreased from 7.73 1.35 to 3.40 1.65 (p< 0.001).

TABLE 1. The initial comparison of all Knee Injury and Osteoarthritis Outcome Score (KOOS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) related variables between baseline and 12-months follow up (mean ± standard deviation)

Clinical score	Baseline	12-months follow up	*P* (paired)	Average percent change
KOOS Pain_1	38.69 ± 17.34	64.57 ± 15.38	<0.001	+66.9
KOOS Symptom_1	47.76 ± 17.88	69.84 ± 15.91	<0.001	+46.2
KOOS ADL_1	39.6 ± 19.5	64.25 ± 17.84	<0.001	+62.2
KOOS Sport/Rec_1	16.25 ± 15.55	34.69 ± 20.85	0.003	+113.5
KOOS QOL_1	13.28 ± 12.68	36.7 ± 19.24	<0.001	+176.4
WOMAC PAIN_1	11.88 ± 3.76	6.5 ± 3.35	<0.001	-45.3
WOMAC STIFFNESS_1	4.31 ± 1.89	2.56 ± 1.46	0.001	-40.6
WOMAC PHYSICAL FUNCTION_1	39.19 ± 14.2	23.19 ± 10.85	<0.001	-40.8
WOMAC TOTAL SCORE_1	55.38 ± 18.83	32.25 ± 14.62	<0.001	-41.8
VAS resting_1	4.06 ± 2.35	0.75 ± 1.65	<0.001	-81.5
VAS movement_1	7.38 ± 1.41	3.38 ± 1.89	<0.001	-54.2

Conclusions of the authors:

- The positive effects of autologous and MFat injection employed intra-articularly, most likely via trophic and immunomodulatory mechanisms, induce host chondrocytes to proliferate and to produce an extracellular matrix that consequently influences structural and biochemical changes in the cartilage.
- Moreover, our data suggests that **increased GAG production directly influences hyaline cartilage quality**, rather than cartilage thickness.
- We were not able to show that areas of complete cartilage destruction with exposed bone within knee joints were covered with newly-formed cartilage at the end of the 12-month period.
- Major effects of the treatment within our study as measured with dGEMRIC MRI could be observed in the areas of the knee joint where some residual cartilage tissue thickness was present at baseline.

[1]*Hudetz et al, Genes 2017, 8, 270,*
[2]*Boric et al, Genes 2019, 10, 1051*
[2]*Hudetz et al, 11th ISABS conf. 2019*

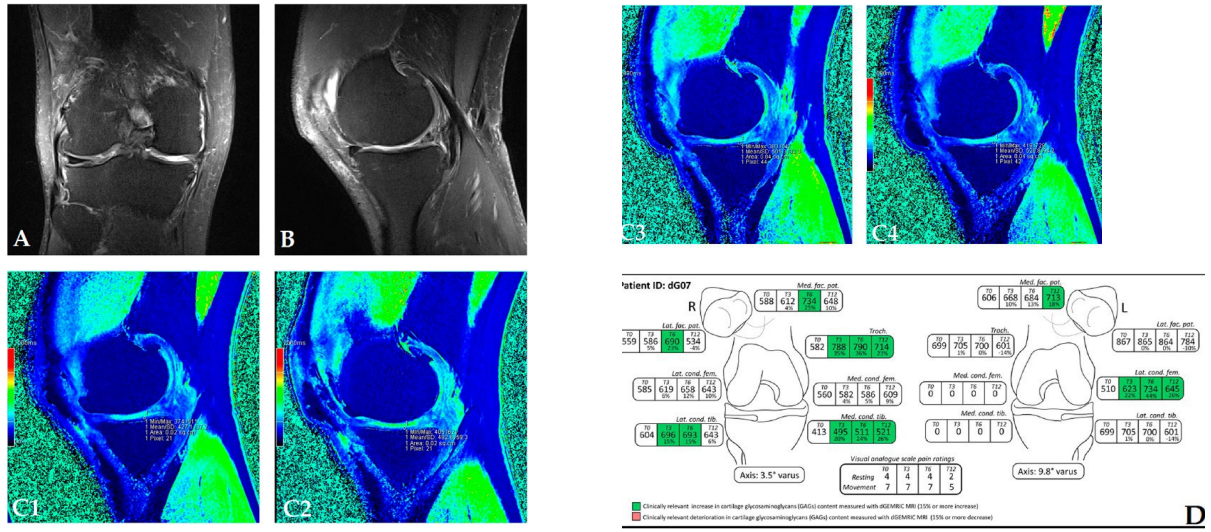
Standalone Inj. – Pilot study in Severe Knee OA with 24 months FU (3/3)[1,2,3]

Objective:

- Evaluate the effects of a standalone Lipogems injection on cartilage extracellular matrix and content of proteoglycans in osteoarthritic cartilage (KL 3 and 4).

Conclusion:

- After 12 months increased glycosaminoglycan (GAG) content in hyaline cartilage (measured by dGEMRIC MRI), in line with the observed improvement in VAS and clinical results.
- Over half of the measurements showed significant GAG improvement 24 months after intra-articular injection, opposed to the expected GAG decrease over the natural course of the disease



Patient case.

- Coronal (A) and sagittal (B) MRI show complete loss of articular cartilage of the medial femoral and tibial condyles (ICRS grade IV chondromalacia), thinning and shallow fissures of the articular cartilage in the lateral femoral and tibial condyles (ICRS grade IV chondromalacia), edge osteophytes and joint effusion.
- (C1–C4). The MRI with the dGEMRIC index values at four-time points (T0: baseline; T3: three months after injection; T6: six months after injection; T12: 12 months after injection).
- (D) The scheme of the dGEMRIC index with different joint facets throughout the study period at T0, T3, T6 and T12 combined with VAS scale ratings in T0, T3, T6, T12.

[1]*Hudetz et al, Genes 2017, 8, 270,*
[2]*Boric et al, Genes 2019, 10, 1051*
[2]*Hudetz et al, 11th ISABS conf. 2019*

Standalone Inj.– Pilot study in Severe Knee OA[1]

Study Design:

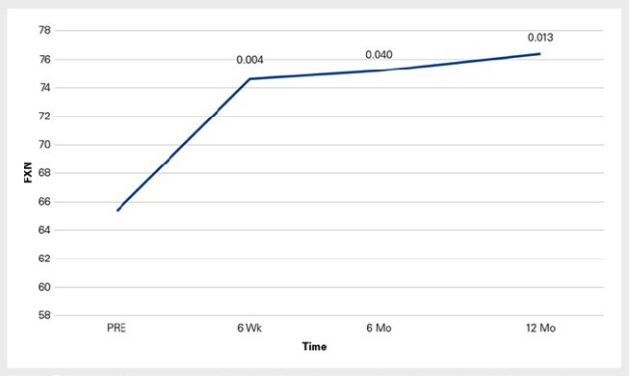
- A prospective, non-randomized, clinical trial of a single intra-articular injection of Lipogems tissue under ultrasound guidance
- 17 patients enrolled, 26 symptomatic knees assessed
- Kellgren-Lawrence grade: III/IV, refractory to conservative therapies, candidates for Total Knee Arthroplasty (TKA)
- New Jersey Regenerative Institute, Rutgers Medical School

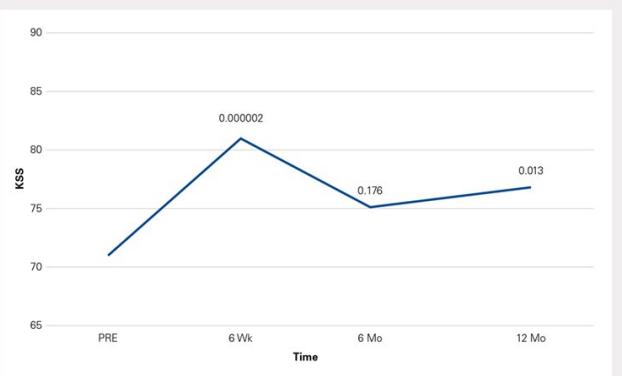
Endpoints:

- **Safety:** Adverse reactions were monitored throughout the study
- **Efficacy:** Clinical evaluation using the numerical pain rating scale (NPRS), the 100-point Knee Society Score (KSS), including functional component (FXN), and the lower extremity activity scale (LEAS) at 6 weeks, 6 months, and 12 months

Results evaluation :

- **Safety**: No significant adverse events were reported in the subjects of this study.
- **Efficacy:**
  - Significant improvement that was noted at 6 weeks was maintained through 12 months after the treatment in all scales, including the NPRS, the KSS, and the FXN beginning at 3 months and continuing through 12 months.
  - The LEAS was statistically significant through 6 months after the treatment but not significant at 12 months





Outcome Measures: FXN (Functional score); KSS (Knee Society Score)

Conclusion:

- The procedure appears to be a safe and effective treatment option in patients with refractory severe (grade 3 or 4) knee OA.
- This study showed significant improvements in pain, quality of life, and function for at least 12 months in this study population.
- This intervention may represent a nonsurgical treatment option to avoid knee joint replacement in this population

[1]Panchal, Malanga, Sheinkop, Am J Orthop. 2018; 47(11)

Inject. + Surgery - RCT on Knee Focal Chondral Lesions [1]

Study Purpose and Design:

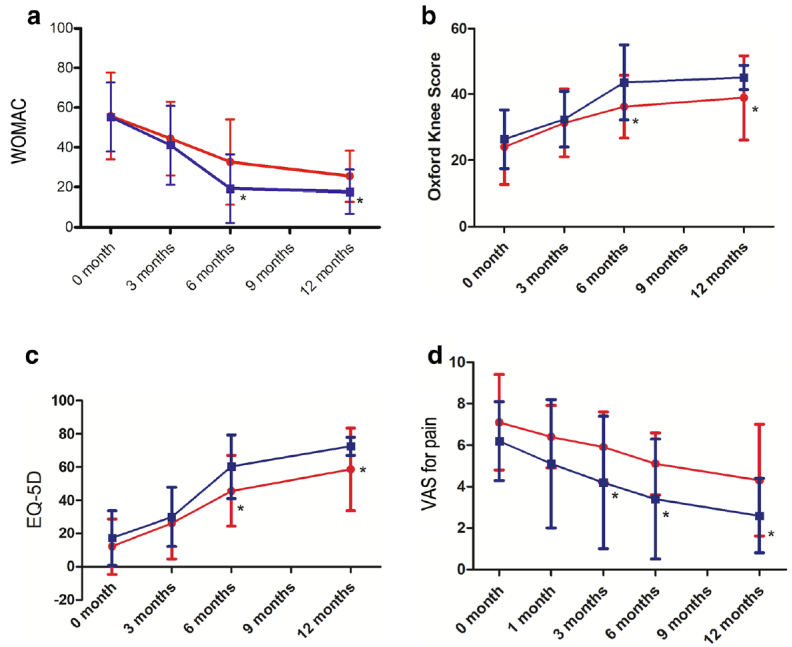
- Does MFat improve functional outcomes in patients undergoing microfracture to treat focal chondral lesions compared to microfracture alone?
- All patients underwent microfracture to treat focal chondral lesion defects; patients in the treatment group received and intra-articular injection of MFat following the procedure. Functional patient reported outcomes (PRO), safety and post-surgical drug consumption data were collected over a 1yr timeframe.
- Prospective RCT, microfracture +/- MFat, N=20/20

Endpoints:

- Primary: Western Ontario & McMaster Universities Osteoarthris Index (WOMAC)
- Secondary: adverse events, Oxford Knee Score, EQ-5KD, VAS, analgesics and anti-inflammatory consumption
- Data were collected at 3, 6, 9- and 12-month time points and compared to pre-op measurements

Results:

- No adverse events or difference in drug consumption were noted across both groups
- At 3 months, all patients showed improvements from baseline with the treatment group demonstrating significantly lower VAS scores.
- At 6 and 12 months, patients receiving MFat showed significant improvement on all outcome measures compared to the control group.



Temporal trends of scores for WOMAC, KOOD, EQ-5D and VAS in experimental group (blue line) and control group (red line)

- MFat in conjunction with microfracture is safe and more effective than microfractures alone in patients with focal chondral defect lesions.

1 Bisicchia, S., Bernardi, G., Pagnotta, S. M. & Tudisco, C. Micro-fragmented stromal-vascular fraction plus microfractures provides better clinical results than microfractures alone in symptomatic focal chondral lesions of the knee. Knee Surgery, Sport. Traumatol. Arthrosc. (2019). doi:10.1007/s00167-019-05621-0

Inject. + Surgery - Pilot study with three year follow up in Knee OA [1]

Study Design:

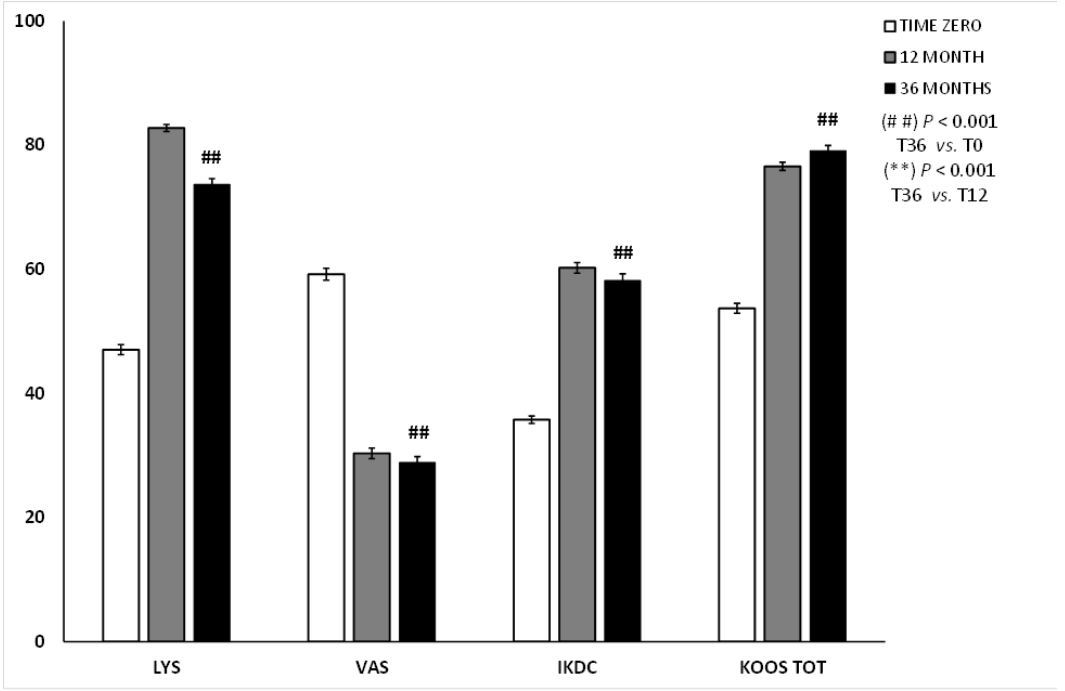
- Diffuse degenerative knee osteoarthritis (grade II, III and IV)
- LIPOGEMS, intra-articular injection **during Arthroscopy**
- Observational study, 30 patients enrolled (29 observed at 36 months)
- Negrar hospital (Verona, Italy)

Endpoints:

- **Safety:** type and incidence of any adverse event during 36 months
- **Efficacy:** KOOS, IKDC-subjective, Tegner Lysholm Knee, and VAS pain scales at T0, 12 months, 36 months follow-up (10 points of improvement in the scores considered clinically significant)

Results evaluation :

- **Safety**: no adverse events, lipodystrophy cases at the harvesting site nor atypical inflammatory reactions at the joint level were reported in the 3 year period for all the 29 patients
- **Efficacy**:
  - 12 months:
    - No patient underwent additional treatment.
    - Median improvement of 20 points observed in IKDC-subjective and total KOOS, higher percentage of success in VAS pain and Tegner Lysholm Knee, (total median improvement was 24 and 31 points, respectively).
  - 36 months:
    - 7 patients underwent additional treatment (other injections of HA, PRP, ..)
    - 22 patients that had no other treatments in the 3 year period showed that the results observed at 1 year follow-up were maintained (T36 vs. T12, p>0.05).
    - 41%, 55%, 55%, and 64% of the patients improved with respect to the 1-year follow-up in the Tegner Lysholm Knee, VAS, IKDC-subjective and total KOOS, respectively.
    - Compared to pre-operative values, more than 50% of the patients improved at least 20 points in all the considered scores, and 55% of the patients improved at least 30 points in the VAS pain scale



Conclusion:

- Results point to autologous and micro-fragmented adipose tissue injection as an innovative and safe approach for the management of diffuse degenerative knee chondropathy in the long-term
- Notably, the results have been maintained at 3 years with no significant differences in all the evaluated parameters with respect to the 1-year follow up assessment

[1]Russo et al. Journal of Experimental Orthopaedics (2017) 4:33, Russo et al, Journal of Experimental Orthopaedics (submitted)

Inject. + Surgery - Pilot study in Severe Knee OA

Study Design:

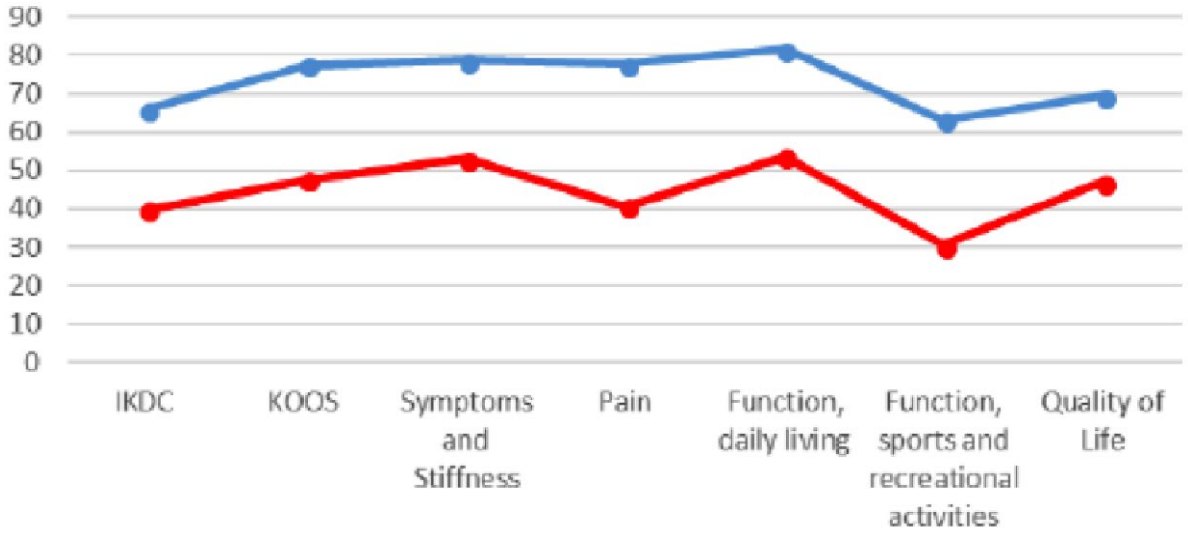
- Severe Knee osteoarthritis
- MFat, intra-articular injection associated with arthroscopy debridement
- Observational study, 43 patients enrolled, 2 with grade III and 41 with grade IV (Kellgren Lawrence scale)
- University of Modena - Reggio Emilia (UNIMORE) hospital

Endpoints:

- **Safety:** type and incidence of any adverse event during 12 months
- **Efficacy:** KOOS, IKDC-subjective scales at T0, 12 months

Results evaluation :

- **Safety**: no adverse events reported in the 1-year FU
- **Efficacy:**
  - 2 patients underwent a knee replacement in the FU
  - In the remaining 41 cases, the average IKDC (65.97) and KOOS (77.46) had a significant improvement at 1 year with respect to the pre-operative average scores (IKDC 39.75 and KOOS 47.52)
    - 16 patients had GOOD/EXCELLENT results (KOOS>80, IKDC>70)
    - 23 patients had MODERATE results (KOOS 60-80, IKDC 50-70)
    - 2 patients had SUFFICIENT results (KOOS<60, IKDC<50)
      - Both patients experienced challenges with adipose harvesting (25 cc required) due to insufficient fat resources (i.e., underweight).



IKDC, KOOS scores and KOOS sub-scores at pre-op (red) and 1 year (blue)

Conclusion:

- Results show the safety and potential benefit of autologous and micro-fragmented Lipogems adipose tissue injection.
- This proved to be a simple, fast, minimally invasive and single-step treatment in association with arthroscopy debridement (which is reported to achieve no better results than placebo when administered alone)

A. Benoni, F. Catani (unpublished)

Inject. + Surgery – Pilot study in medium Knee OA[1]

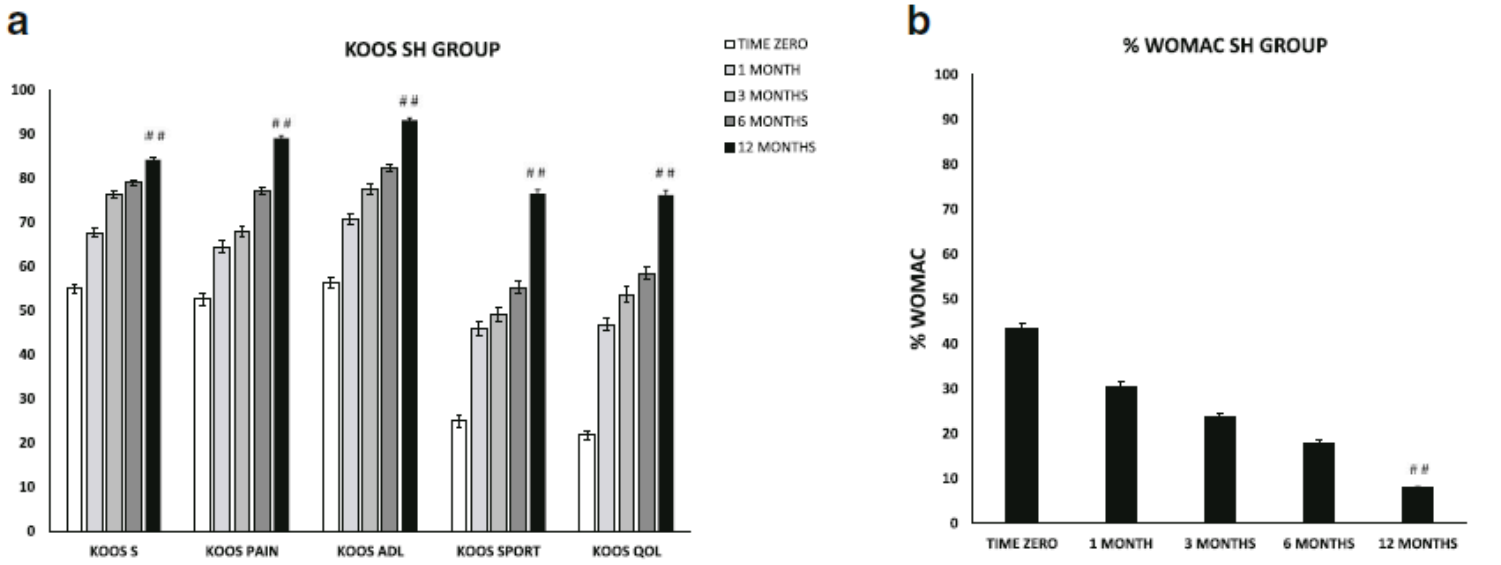
Study Design:

- A retrospective interventional, single-center, open label clinical trial of an arthroscopic procedure (chondral shaving) associated with an injection of Lipogems
- Thirty-five patients affected by symptomatic knee osteoarthritis were treated. 14 of the patient, with a meniscal damage, received an associated meniscectomy
- Kellgren-Lawrence grade: I-III
- Spotorno Foundation c/o San Michele Clinics, Albenga (Italy)

Results evaluation :

- **Safety**:
  - No adverse events nor relevant complications were recorded.

- **Efficacy:**
  - Clinical outcomes 1, 3, 6, and 12 months follow-up using Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire
  - A steady and statistically significant improvement of all the clinical scores from pre-operative evaluation to 1,3, 6, and 12 months follow-up was observed. KOOS sport and quality of life being the most improved scores.
  - 92% of the patients clinically improved and 100% of them were satisfied with the treatment.



Trend of functional improvements from baseline to 12 months' follow-up. Results are expressed as mean and standard error. A $p < 0.05$ (T12 vs. T0) was considered statistically significant (# #). a KOOS score. KOOS S = symptoms; KOOS P = pain; KOOS ADL = activity daily living; KOOS Spt = sport; KOOS QoL = quality of life. b WOMAC Index.

Conclusion

- The result of the study pointed to micro-fragmented adipose tissue as a safe and beneficial adjuvant in the surgical treatment of degenerative knee chondropathy. The procedure is simple, sustainable, quick, minimally invasive, one-step, and safe.
- After one year, the results are very satisfactory and promising.

[1]*Cattaneo et al. BMC Musculoskeletal Disorders (2018) 19:176*

Inject. + Surgery – Pilot study in medium Knee OA[1]

Preliminary results of autologous adipose-derived stem cells in early knee osteoarthritis: identification of a subpopulation with greater response

Alfredo Schiavone Panni[1] · Michele Vasso[1] · Adriano Braile[1] · Giuseppe Toro[1] · Annalisa De Cicco[1] · Davide Viggiano[2] · Federica Lepore[1]

Abstract

Purpose The purpose of this study was to report the clinical and functional results of a series of patients with early knee osteoarthritis (KOA) treated with the intra-articular injection of autologous adipose-derived stem cells (aASCs) plus arthroscopic debridement. The hypothesis was that protocol would significantly improve the clinical and functional outcomes in patients with early KOA.

Methods Fifty-two patients with early KOA, who received arthroscopic debridement followed by percutaneous injection of aASCs, were enrolled into the study and retrospectively analyzed with an average follow-up of 15.3 (range, 6 to 24) months. Patients were assessed through the IKS knee and function scores and VAS pain scale.

Results The mean IKS knee score improved from 37.4 (range, 14 to 79) points pre-operatively to 62.6 (range, 27 to 95) points at the latest follow-up ($p < < 0.01$). The mean IKS function score improved from 57.2 (range, 25 to 100) points pre-operatively to 83.0 (range, 35 to 100) points at the latest follow-up ($p < < 0.01$). The mean VAS score decreased from 8.5 (range, 3 to 10) pre-operatively to 5.1 (range, 0 to 8) at the latest follow-up ($p < < 0.01$). Additionally, patients with a pre-operative VAS score greater than 8 were found to show greater clinical and functional benefits compared with patients with VAS score lower than 8.

Conclusions The knee injection of aASCs associated to arthroscopic debridement increased significantly the clinical and functional scores in patients with early KOA at a mid-term follow-up, especially those with higher pre-operative VAS scores.

Mean IKS knee and function and VAS scores

	Preoperatively	*Latest follow-up*	*p value*
Mean IKS knee (points)	37.4 (14–79)	62.6 (27–95)	<< 0.01
Mean IKS function (points)	57.2 (25–100)	83.0 (35–100)	<< 0.01
VAS (points)	8.5 (3–10)	5.1 (0–8)	<< 0.01

Percent improvement of IKS knee and function and VAS scores in patients presenting with high or low pain

	VAS < 8	*VAS > 8*	*p value*
Improvement in IKS knee (% over basal)	26 ± 17%	115 ± 22%	0.005
Improvement in IKS function (% over basal)	22 ± 18%	64 ± 10%	0.05
Improvement in VAS (% over basal)	4 ± 15%	44 ± 4%	0.02

Conclusion:

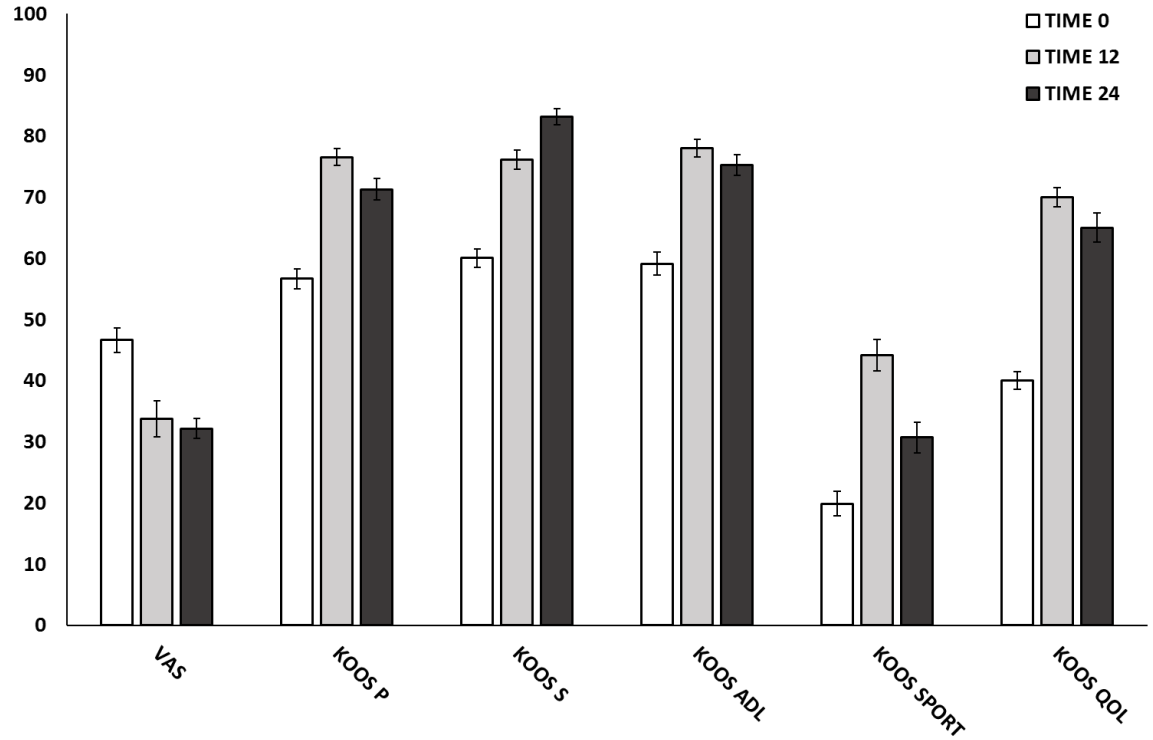
- The injection of MFat associated with arthroscopy (chondral shaving/abrasion and/or meniscal regularization) significantly increased the clinical and functional scores in patients with early knee OA at a mid-term follow-up (6-24 months).
- Significantly higher improvements in patients with pre-operative VAS score > 8.
- No treatment-related adverse events.
- At the latest follow-up, 96.2% of patients expressed satisfaction and reported good/excellent improvements in function and/or pain.

[1]Schiavone Panni et al. International Orthopaedics (2019)

Inject. + Surgery - Knee chondropathy: 2 year follow up[1]

Over **300** procedures with **LIPOGEMS** since **2014**

- Intra-articular injections in osteoarthritis treatment (even to 6 big joints during one procedure; various joints)
- During the surgical procedure:
  - *around the injured ligaments and tendons*
  - *after ACL/PCL reconstruction*
  - *after meniscal suturing*
  - *around the surgical wound*
  - *into the osteotomy gap*



Results

- **Significant increase in KOOS scores -** The improvement of the symptoms occurred few days after treatment and increased steadily throughout the whole period of the study.
- **VAS** (Visual Analog Scale) **PAIN SCALE** decreased from SEVERE to MILD

[1]Dr. Konrad Slynarski – Lekmed Clinic, Warsaw, Poland (unpublished)

Selected Ongoing Randomised Controlled Trials

- **Moderate - KL Stage II-III**
  - *Is Lipogems procedure effective in improving knee symptoms and function?*

- **Antwerp Orthopaedic Centre (Belgium), Prof. Verdonk**
  - Randomized Controlled, Lipogems vs. Saline, injection, 120 pt., KL II/III
  - Endpoints: clinical at 6, 12, 24 months

- **Zealand University Hospital Køge (Denmark), Prof. Blond** and **Copenhagen University Hospital Amager-Hvidovre, (Denmark), Prof. K. Barfod**
  - Randomized Controlled Lipogems vs. saline, injection, 120 pt., KL II/III
  - Endpoints: clinical at 6, 12, 24 months

- **Severe OA - KL Stage III-IV**
  - *Can Lipogems procedure help in TKA postponement or reduce the waiting list for TKA?*

- **The Lincoln Hospital (UK), Prof. Lee**
  - Lipogems injection in 50 pt. in the wait-list for TKA
  - Endpoints: evaluate number of injected pt. undergoing TKA at 1, 2, 5 years (a measure of effectiveness in postponing joint replacement)

- **Policlinico di Modena (Italy), Prof. Catani**
  - Randomized Controlled, Lipogems vs. TKA, injection w/ arthroscopy, approx 120 pt. KL III-IV with TKA indication
  - Endpoints: in definition (clinical evaluation and nr of pt. undergoing TKA)

- **Istituto Ortopedico Galeazzi (Italy), Dr. Ulivi**
  - Randomized Controlled, injection w/ arthroscopy, 78 pt. KL III/IV, 6 months f.u.
  - Endpoints: clinical

- **Lipogems Procedure in Osteoarthritis**

- **Clinical Data and Trials**
  - Knee
  - **Other (Shoulder, Hip)**
  - Clinical Trials and Publications

Shoulder Osteoarthritis – Pilot study with 1 year follow up

Study Design:

- Refractory Shoulder Pain with Osteoarthritis, and Rotator Cuff Tear
- MFat, intra-articular injection under direct ultrasound guidance
- Observational study, 20 patients enrolled (18 observed at 12 months)
- Optimum Joint, Integrated Joint and Spine, Suffern, NY, USA

Endpoints:

- **Safety:** type and incidence of any adverse event during 12 months
- **Efficacy:** Outcomes assessed immediately following treatment, at weeks 1 and 5, months 3, 6 and 12 by Numerical Pain Scale (NPS) and The American Shoulder and Elbow Surgeons Score (ASES).

Results evaluation :

- **Safety**: No post procedural complications or serious adverse events were reported
- **Efficacy**:
  - significant improvement through twelve months in all measured scores
  - The average improvement of NPS was from 7.5 to 3.6 at one year. The average ASES from 33.7 to 69.2 at one year (0-100 scale 100 perfect function)

Conclusions:

- The results from this study demonstrate significant improvements in pain, function disability and quality of life as represented by positive outcomes in all measured scores through twelve months with no adverse events reported.
- The autologous, minimally manipulated, micro-fragmented adipose tissue administered under continuous ultrasound guidance, appears to be safe, effective and produced long term results in the treatment of shoulder pain having multi-factorial origins.

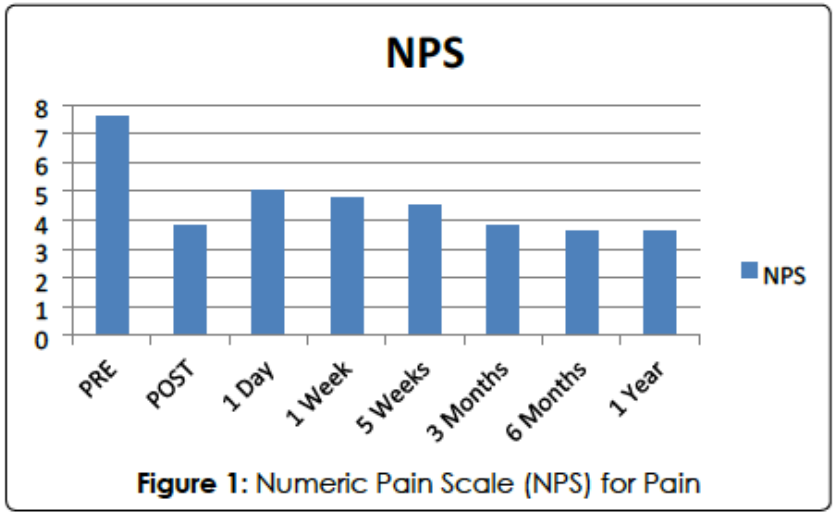


Figure 1: Numeric Pain Scale (NPS) for Pain

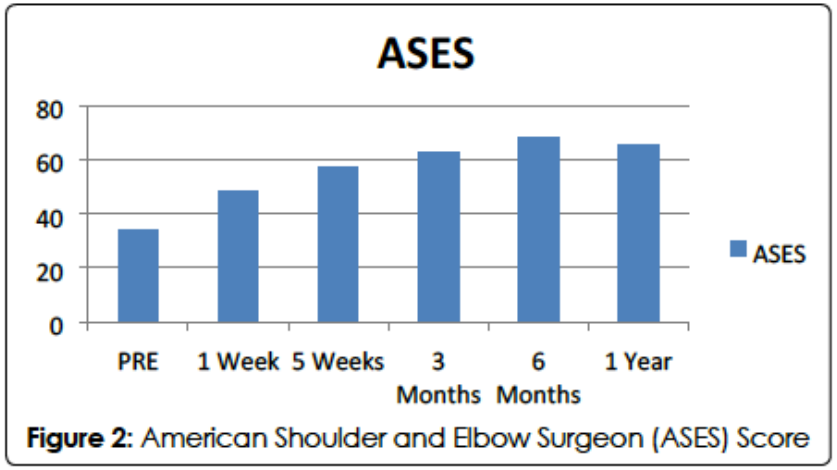


Figure 2: American Shoulder and Elbow Surgeon (ASES) Score

[1]*Striano RD, Malanga GA, Bilbool N, Azatullah K (2018. Orthop Spine Sports Med 2: JOSSM 014*

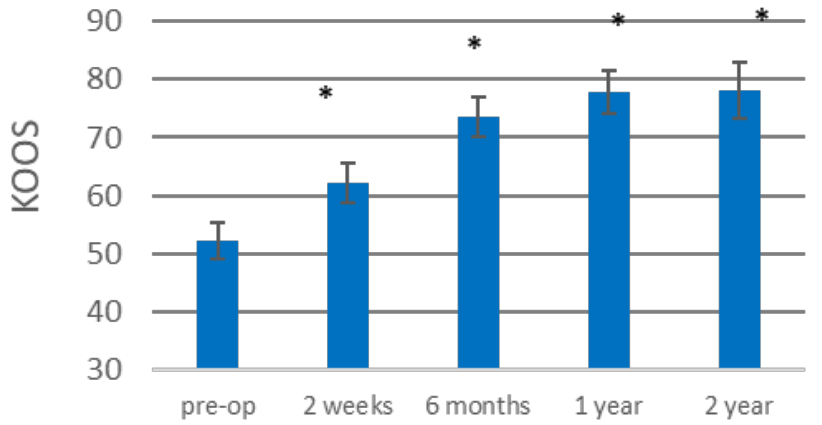
Knee and Shoulder Osteoarthritis – Pilot study with 2 year follow up

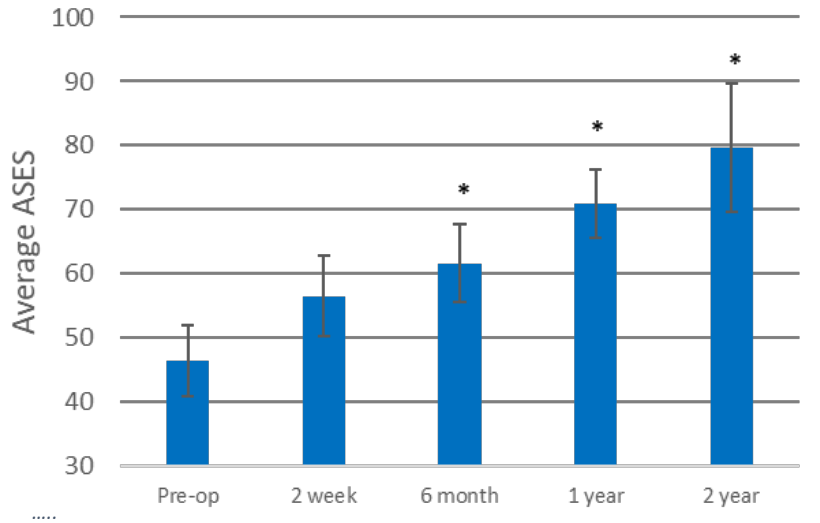
Study Design:
- Patients with radiographic evidence of stage 1-3 K/L (Knee) or Larson (shoulder) scale with or without rotator cuff tear
- LIPOGEMS, intra-articular injection under direct ultrasound guidance
- Observational study, 50 patients enrolled (37 knee, 13 shoulder)
- Advanced Orthopedics and Sports Medicine, Denver, CO

Endpoints:
- **Safety:** type and incidence of any adverse event over 24 months
- **Efficacy:** Outcomes measures: Knee Injury and Osteoarthris Outcomes Score (KOOS) and American Shoulder and Elbow Surgeon's (ASES) score assessed at 2weeks; 6, 12, and 24 months

Results evaluation:
- **Safety**:
  - No post procedural complications or serious adverse events were reported
- **Efficacy**:
  - KOOS: Significant improvements at all time points were maintained through 2 yrs compared to pre-op
  - ASES: Significant improvements at 6, 12 and 24mo time points

Conclusions:
- The results from this study demonstrate significant improvements in pain, function disability and quality of life as represented by positive outcomes in KOOS and ASES through 2 years with no adverse events reported.
- Results demonstrate a maintenance of functional outcomes from the 1 to 2yr time point, with a trend toward improvement in ASES at 2 yrs





Papilion, Interim Data Review, November 2019

Evaluation of autologous micro-fragmented adipose tissue effectiveness in arthroscopic repair of rotator cuff injury

Study Purpose and Design:

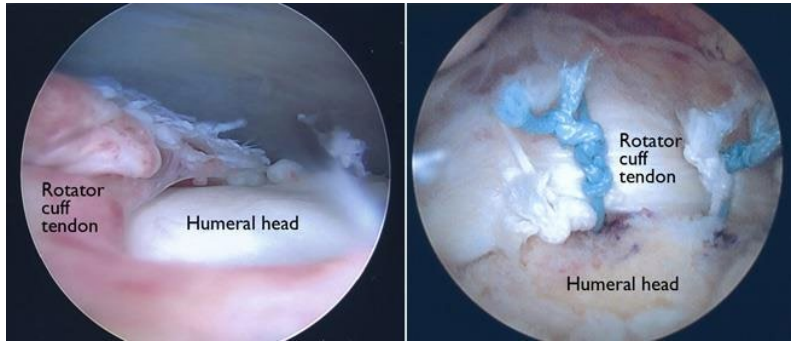
- Does MFat improve functional outcomes in patients undergoing arthroscopic repair of rotator cuff injury compared to rotator cuff repair alone?
- All patients suffering from full depth injuries of the supraspinatus and/or infraspinatus tendon (lesions classified as C1, C2, C3 following Snyder classification) underwent standard arthroscopic repair of the defect, and patients in the treatment group receiving Mfat injections following the repair. Functional patient reported outcomes (PRO), safety and re-tear rate was recorded over a 2-year timeframe.
- Prospective RCT, rotator cuff repair +/- MFat, N=52 (26/26)
- **Primary Investigator**: Dr. Pietro Randelli, Gaetano Pini Hospital (Milan, Italy)

Endpoints:

- **Primary:** Constant scale score
- **Secondary:** VAS, increase in abduction and extra-rotation strength, and quantification of re-injury and fatty degeneration of the supraspinatus (MRI and Fuchs classification) at 1 and 2 years.
- PRO's data were collected 1, 3, 6, 12 and 24 months

Results:

- **Study is fully enrolled, with LPLV in January of 2020.**



Hip Chondral Lesions – Pilot study with 2 year follow up

AAOS/ ORS 2017 Award Winning Presentation

Study Design:

- Acetabular Chondral Lesions
- LIPOGEMS, intra-articular injection under direct ultrasound guidance
- Retrospective comparative analysis, 194 patients, 77 treated with microfracture (MFx) and 117 with Lipogems Injection (MFat) technique, 2 years follow up
- COF Lanzo Hospital, Como (Italy)

Endpoints:

- **Safety:** type and incidence of any adverse event during 24 months
- **Efficacy:** Outcomes assessed by modified Harris Hip Score (mHHS) at 6 months, 1 and 2 years' follow-up

Results evaluation :

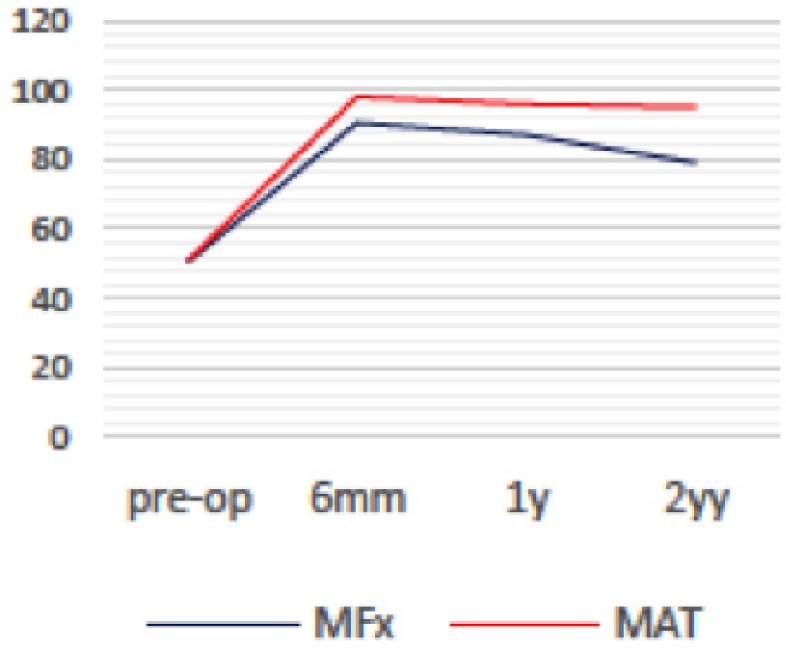
- **Safety**: No related adverse events were reported
- **Efficacy**:
  - Both MFx and MAT significantly improved the clinical status at 6 months and 1 year (mHHS 84±6/MFx - 94±4/MAT).
  - Over the 2 years period, a progressive decrease in functionality was measured in the MFx group, while the positive outcomes of the MAT group remained stable.
  - **No conversion to total hip arthroplasty was observed in the MAT group, whereas THA was necessary in 10 (7.8%) of the patients of the MFx group**.

Conclusions:

- MFx is still the treatment of choice for small chondral defects of the acetabulum and femoral head. Although MFx has been shown to be effective, after a mean of two years a deterioration in the function is reported.
- MAT approach is safe and improves the clinical outcomes when associated with the arthroscopic repair of an acetabular chondral damage. The MAT group showed long-term improvement and scoring significantly better than the MFx group over the 2-year period.

Study Inclusion Criteria:

- Age between 18 and 55 yy.
- Acetabular chondral lesion grade III and IV.
- Chondral lesions size 2-8 cm2.
- radiological degenerative changes < 2 (Tonnis class).



Inclusion Criteria and evolution of the average mHHS score vs. FU time for the two arms of the study

[1]A. Fontana, AAOS 2017

- **Lipogems Procedure in Osteoarthritis**

- **Clinical Data and Trials**
  - Knee
  - Other (Shoulder, Hip)
  - **Clinical Trials and Publications**

Ongoing Investigator Initiated Clinical Studies (US and EU)

- **Knee Pathologies**
  - Level 1 RCTs: 8
  - Prospective: 10
  - Retrospective: 2
- **Shoulder**:
  - Level 1 RCTs: 3
  - Prospective: 3
- **Other Ortho/Gen Surgery**
  - Prospective: 3
- **New Investigator Initiated Studies**:
  - Prospective: 7
  - Retrospective: 2

Osteoarthritis – Ongoing RCT Studies (1/2)

Q1/Q2 2020

P. Investigator	Center	Country	Pathology	Study Type	Description	Nr of Patients	Follow Up Time	Status
S. Zaffagnini	Orthopedic Institute Rizzoli, Bologna	IT	Knee OA	Randomized Controlled Lipogems vs. PRP	Injection only 1. INTERVENTION: one intra articular injection of Lipogems 2. CONTROL: one intra articular injection of PRP	118 (59 per arm)	12 and 24 months	Ongoing - Presented 6 months partial data at SIGASCOT 2019. All patients ttreated and reached the last endpoint.
P. Randelli	Istituto Ortopedico G. Pini, Milan	IT	Shoulder Rotator cuff repair	Randomized Controlled arthroscopy ± Lipogems	Arthroscopy 1. INTERVENTION: rotator cuff repair associated with Lipogems 2. CONTROL: rotator cuff repair alone	52 (26 per arm)	24 months	Ongoing - All patients treated.By March 2020, last patients FU at 24months completed. Expecteing to submit pubvlication by May 2020
D. Richter	University of New Mexico	USA	Knee OA	Randomized Controlled Lipogems vs. steroids vs. placebo	Injection only ARM 1: one intra articular injection of Lipogems ARM 2: one intra articular injection of steroids ARM 3: one intra articular injection of placebo	84 (28 per arm)	6 months	Ongoing (presented partial 6 mo data at Vail conference in August 2019)
M. Ulivi	Orthopedic Institute Galeazzi - Milan	IT	Knee OA (KL 3 and 4)	Randomized Controlled arthroscopy ± Lipogems	Arthrorcopy 1. INTERVENTION: arthroscopy associated with Lipogems 2. CONTROL: arthroscopy alone	78 (39 per arm)	6 months	Ongoing

….. Plus the retrospective analysis of a Clinical Database of over 1,700 patients with knee OA with up to 5 years follow up.

Osteoarthritis – Ongoing RCT Studies (2/2)

H2 2020-.....

P. Investigator	Center	Country	Pathology	Study Type	Description	Nr of Patients	Follow Up Time	Status
T. Vangsness	USC	USA	Knee OA	Randomized Controlled Lipogems vs. Hyaluronic acid	Injection only 1. INTERVENTION: one intra articular injection of Lipogems 2. CONTROL: one intra articular injection of HA	54 patients (27 per arm)	12 months	Ongoing
E. Arnaldi	Humanitas Clinical Institute, Milan	IT	Knee OA (KL 3 and 4)	Prospective Observational	Injection only	20	12 months	Ongoing
P. Lee	The Lincoln Hospital/Leicester Hospital	UK	Knee TKA	Prospective Interventional	Injection only Patients in the waiting list for TKA will be treated with 1 single Lipogems injection and evaluated at 2 and 6 weeks, 3 and 6 months, 1, 2, 5 years with Oxford Knee Score, VAS pain and EQ-5D. Results will be compared with an historic cohort data of TKA .	50	2 and 6 weeks 3 and 6 months 1, 2, 5 years	Ongoing – Expcting to have 40 patients treated by Sept end
L. Blond and K. Barfod	Zealand University Hospital Køge Copenhagen University Hospital Amager-Hvidovre	DENMARK	Knee OA	Randomized Controlled Single-blind Multicenter Lipogems vs. placebo	Injection only 1. INTERVENTION: one intra articular injection of Lipogems 2. CONTROL: one intra articular injection of placebo (saline) At 6 months follow up patients who experience failure of the treatment are treated again: patient who were treated with placebo at baseline are treated with Lipogems harvested at baseline and stored for later implantation at -81°C. Patients who were treated with Lipogems at baseline are treated with placebo. In this way, the patients are still blind to the intervention at 12 months follow up.	120 (60 per arm)	6 months (1° endpoint)	Ongoing – 40 patients treated as of Sept 2019. Planning to complete treatmnet within 2020. Final publication expected not earlier than 2021
P. Verdonk	Antwerp Orthopaedic Center (Monica Hospitals)	BELGIUM	Knee OA	Randomized Controlled Lipogems vs. HA	Injection	50 patients per arm	12 months	Ongoing. First patient treated Sept 2019
F. Catani	Università di Modena Reggio Emeilia	IT	Knee OA (KL 3 and 4)					Ongoing

Lipogems in OA - Clinical Publications (1/4)

KNEE

- Bisicchia S, Bernardi G, Pagnotta SM, Tudisco C. Micro-fragmented stromal-vascular fraction plus microfractures provides better clinical results than microfractures alone in symptomatic focal chondral lesions of the knee. Knee Surgery, Sport Traumatol Arthrosc. July 2019. doi:10.1007/s00167-019-05621-0
- Malanga GA, Bemanian S. Microfragmented adipose injections in the treatment of knee osteoarthritis. J Clin Orthop Trauma. 2019;10(1):46-48. doi:10.1016/j.jcot.2018.10.021
- Hudetz D, Borić I, Rod E, et al. Early results of intra-articular micro-fragmented lipoaspirate treatment in patients with late stages knee osteoarthritis: a prospective study. Croat Med J. 2019;36(60):227.
- Polancec, Zenic, Hudetz, et al. Immunophenotyping of a Stromal Vascular Fraction from Microfragmented Lipoaspirate Used in Osteoarthritis Cartilage Treatment and Its Lipoaspirate Counterpart. Genes (Basel). 2019;10(6):474. doi:10.3390/genes10060474
- Mautner K, Bowers R, Easley K, Fausel Z, Robinson R. Functional Outcomes Following Microfragmented Adipose Tissue Versus Bone Marrow Aspirate Concentrate Injections for Symptomatic Knee Osteoarthritis. Stem Cells Transl Med. July 2019. doi:10.1002/sctm.18-0285
- Bisicchia S, Bernardi G, Pagnotta SM, Tudisco C. Micro-fragmented stromal-vascular fraction plus microfractures provides better clinical results than microfractures alone in symptomatic focal chondral lesions of the knee. Knee Surgery, Sport Traumatol Arthrosc. July 2019. doi:10.1007/s00167-019-05621-0
- Schiavone Panni A, Vasso M, Braile A, et al. Preliminary results of autologous adipose-derived stem cells in early knee osteoarthritis: identification of a subpopulation with greater response. Int Orthop. 2019;43(1):7-13. doi:10.1007/s00264-018-4182-6
- Polancec, Zenic, Hudetz, et al. Immunophenotyping of a Stromal Vascular Fraction from Microfragmented Lipoaspirate Used in Osteoarthritis Cartilage Treatment and Its Lipoaspirate Counterpart. Genes (Basel). 2019;10(6):474. doi:10.3390/genes10060474
- Senesi L, De Francesco F, Farinelli L, et al. Mechanical and enzymatic procedures to isolate the stromal vascular fraction from adipose tissue: Preliminary results. Front Cell Dev Biol. 2019;7. doi:10.3389/fcell.2019.00088
- Malanga GA, Bemanian S. Microfragmented adipose injections in the treatment of knee osteoarthritis. J Clin Orthop Trauma. 2019;10(1):46-48. doi:10.1016/j.jcot.2018.10.021
- Russo A, Screpis D, Di Donato SL, Bonetti S, Piovan G, Zorzi C. Autologous micro-fragmented adipose tissue for the treatment of diffuse degenerative knee osteoarthritis: an update at 3 year follow-up. J Exp Orthop. 2018;5(1). doi:10.1186/s40634-018-0169-x

Lipogems in OA - Clinical Publications (2/4)

- Zeira O, Scaccia S, Pettinari L, et al. Intra-Articular Administration of Autologous Micro-Fragmented Adipose Tissue in Dogs with Spontaneous Osteoarthritis: Safety, Feasibility, and Clinical Outcomes. Stem Cells Transl Med. 2018;7(11):819-828. doi:10.1002/sctm.18-0020
- Cattaneo G, De Caro A, Napoli F, Chiapale D, Trada P, Camera A. Micro-fragmented adipose tissue injection associated with arthroscopic procedures in patients with symptomatic knee osteoarthritis. BMC Musculoskelet Disord. 2018;19(1). doi:10.1186/s12891-018-2105-8
- Panchal J, Malanga G, Sheinkop M. Safety and Efficacy of Percutaneous Injection of Lipogems Micro-Fractured Adipose Tissue for Osteoarthritic Knees. Am J Orthop (Belle Mead NJ). 2018;47(11). doi:10.12788/ajo.2018.0098
- Moorman CT, Owusu-Akyaw KA, Godin J, Pecchia S, Oldweiler A. Adipose-derived Mesenchymal Stem Cells and Arthroscopic Surgery. Duke Orthop J. 2017;7(1):34-38. doi:10.5005/jp-journals-10017-1079
- Striano RD, Battista V, Bilboo N. Non-Responding Knee Pain with Osteoarthritis, Meniscus and Ligament Tears Treated with Ultrasound Guided Autologous, Micro-Fragmented and Minimally Manipulated Adipose Tissue. Open J Regen Med. 2017;06(02):17-26. doi:10.4236/ojrm.2017.62002
- Russo A, Condello V, Madonna V, Guerriero M, Zorzi C. Autologous and micro-fragmented adipose tissue for the treatment of diffuse degenerative knee osteoarthritis. J Exp Orthop. 2017;4(1):33. doi:10.1186/s40634-017-0108-2
- Hudetz D, Borić I, Rod E, et al. The effect of intra-articular injection of autologous microfragmented fat tissue on proteoglycan synthesis in patients with knee osteoarthritis. Genes (Basel). 2017;8(10). doi:10.3390/genes8100270

- Striano RD, Battista V, Bilboo N. Non-Responding Knee Pain with Osteoarthritis, Meniscus and Ligament Tears Treated with Ultrasound Guided Autologous, Micro-Fragmented and Minimally Manipulated Adipose Tissue. Open J Regen Med. 2017;06(02):17-26. doi:10.4236/ojrm.2017.62002
- Moorman CT, Owusu-Akyaw KA, Godin J, Pecchia S, Oldweiler A. Adipose-derived Mesenchymal Stem Cells and Arthroscopic Surgery. Duke Orthop J. 2017;7(1):34-38. doi:10.5005/jp-journals-10017-1079

- Sciarretta FV, Ascani C, Fossati C, Campisi S. LIPO-AMIC: technical description and eighteen pilot patients report on AMIC ® technique modified by adipose tissue mesenchymal cells augmentation. G Ital di Ortop e Traumatol. 2017.
- Franceschini M, Castellaneta C, Mineo G. Injection of autologous micro-fragmented adipose tissue for the treatment of post-traumatic degenerative lesion of knee cartilage : a case report. CellR4. 2016;4(1):1-6.

Lipogems in OA - Clinical Publications (3/4)

SHOULDER

- Dyson-Hudson T, Malanga G, Cherian C, Hogaboom NS, Michalec M, Kirshblum S. Ultrasound-Guided, Autologous, Micro-Fragmented Adipose Tissue Injection for Chronic, Recalcitrant Shoulder Pain in Manual Wheelchair Users with SCI.; 2019.
- Hogaboom NS, Malanga GA, Dyson-Hudson T. Supraspinatus Tendon Signal Intensity after Micro-Fragmented, Autologous Adipose Tissue Treatment in a Wheelchair User with Paraplegia: A Case Study.; 2019.
- Cherian C, Malanga GA, Hogaboom N, Pollack MA, Dyson-Hudson TA. Autologous, Micro-Fragmented Adipose Tissue as a Treatment for Chronic Shoulder Pain in a Wheelchair Using Individual with Spinal Cord Injury: A Case Report. Spinal Cord Ser Cases. 2019;5.
- Striano, Richard D, Gerard A Malanga, Norma Bilbool KA. Refractory Shoulder Pain with Osteoarthritis, and Rotator Cuff Tear, Treated With Micro-Fragmented Adipose Tissue. J Orthop Spine Sport Med. 2018;2:1 014.
- Striano R, Bilbool N, Azatullah K, Hilado J. Non-Responsive Shoulder Pain with Osteoarthritis , Rotator Cuff Tear and Labral Tear Treated With Autologous Micro-Fragmented Adipose Tissue Under Continuous Ultrasound Guidance.; 2018.
- Striano RD, Malanga GA, Shiple BJ, Bilbool N, Azatullah K. Non-Responsive Multi-Factorial Shoulder Pain With Osteoarthritis, Rotator Cuff Tear, Tendinopathies, and or Labral Tear Treated With Autologous, Minimally Manipulated, Micro-Fragmented Adipose Tissue Under Continuous Ultrasound Guidance.; 2018.
- Moorman CT, Owusu-Akyaw KA, Godin J, Pecchia S, Oldweiler A. Adipose-derived Mesenchymal Stem Cells and Arthroscopic Surgery. Duke Orthop J. 2017;7(1):34-38. doi:10.5005/jp-journals-10017-1079

Lipogems in OA - Clinical Publications (4/4)

HIP

- Dall'Oca C, Breda S, Elena N, Valentini R, Samaila EM, Magnan B. Mesenchymal stem cells injection in hip osteoarthritis: Preliminary results. Acta Biomed. 2019;90:75-80. doi:10.23750/abm.v90i1-S.8084
- Jannelli E, Fontana A. Arthroscopic treatment of chondral defects in the hip: AMIC, MACI, microfragmented adipose tissue transplantation (MATT) and other options. SICOT-J. 2017;3:43.
- Fontana A. Adipose Tissue Derived Mesenchymal Stem Cell Therapy for the Treatment of Chondral Lesions in The Hip. A 2 Years Follow-up Comparison Study with Microfractures.; 2016.
- Freeman CR, Azzam MG, Leunig M. Hip preservation surgery: surgical care for femoroacetabular impingement and the possibility of preventing hip osteoarthritis. J Hip Preserv Surg. 2014;1(2):46-55.

TALUS

- D'Ambrosi R, Indino C, Maccario C, Manzi L, Usuelli FG. Autologous microfractured and purified adipose tissue for arthroscopic management of osteochondral lesions of the talus. J Vis Exp. January 2018. doi:10.3791/56395

ANKLE

- Kennedy JG. Arthroscopic Debridement and Micronized Adipose Tissue Injection for End-Stage Ankle Arthritis.; 2018.

SPINE

- Grossi P, Giarratana S, Cernei S, Grossi S, Doniselli FM. Low back pain treated with disc decompression and autologous micro-fragmented adipose tissue : a case report. CellR4. 2016;4(1):4-9.