Abstract OP0058 – Responders over time with 95%CI

Abstract OP0058 – Table 1

	Hand OA		Knee OA	
	LD-RT (n=28)	Sham (n=28)	LD-RT (n=27)	Sham (n=28)
Male/Female, n	4/24	8/20	12/15	15/13
Age (years)	67 (1)	62 (12)	62 (9)	68 (9)
BMI (kg/m ²)	26 ²⁴⁻²⁷	29 ²⁵⁻³¹	29 ²⁵⁻³⁰	26 ²⁴⁻³¹
Pain (0–100) #	54 (19)	56 (15)	41 (14)	39 (17)
Functioning (0–100) #	55 (25)	59 (16)	40 (17)	38 (19)
Effusion*	6 ⁵⁻⁸	5 ³⁻⁸	6 ⁵⁻⁸	5 ⁴⁻⁷
Synovial thickening*	3 ¹⁻⁴	1 ¹⁻³	2 ¹⁻³	2 ¹⁻³
Power Doppler*	1 [0–2.5]	1 [0–3]	NA	NA
MRI effusion/synovitis (0–12)	NA	NA	5 ²⁻⁸	4 ²⁻⁷

Mean (sd) or median [25%–75%]; lower scores indicate better health status

#: AUSCAN or WOMAC, respectively; * Hand: joint count (0–18), Knee: thickness (mm); NA: not assessed

Methods: Patients with hand OA (n=56) or knee OA (n=55) according to ACR-criteria, with a pain score $\geq 5/10$, not responding to analgesics and exercise therapy were included. They were randomly allocated 1:1 to the LD-RT (6 × 1 Gy LD-RT in two weeks) or sham (6 × 0 Gy in two weeks) intervention, stratified for pain score (<8 vs ≥ 8). The primary outcome was the number responders according to the OMERACT-OARSI responder criteria, 3 months post-intervention. Secondary outcomes were inflammatory aspects assessed by ultrasound (US; both knee and hand) and MRI (knee only). In hand OA, joints were scored semi-quantitatively (0–3) for US effusion, synovial thickening and power Doppler signal. In knee OA, we assessed the mean US effusion and synovial thickness (mm) at three locations, and the summed MRI effusion/synovitis (semi-quantitatively; 0–3) from four locations. Logistic and linear regression analyses were used to assess differences in dichotomous and continuous outcomes, respectively. Analyses were adjusted for pain stratum.

Results: Baseline characteristics are shown in table 1. The proportion of responders over time is shown in figure 1. After 3 months, in hand OA, there were 8 (29%) responders in the LD-RT group and 10 (36%) in the sham group (OR 0.69; 95% CI: 0.22 to 2.17). In knee OA, there were 12 (44%) responders in the LD-RT

group and 12 (43%) in the sham group (OR 1.09; 95% CI: 0.37 to 3.19). In both hand and knee OA, no significant changes in clinical outcomes and inflammatory aspects were observed in both groups.

Conclusions: We were unable to demonstrate a beneficial effect of LD-RT on pain and functioning, nor on inflammatory processes, in patients with hand or knee OA. In light of absence of other high-level evidence, we advise against the use of LD-RT as treatment for hand and knee OA.

Dutch Trial Register: NTR4574

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2008

OP0059 EFFICACY AND SAFETY OF INTRA-ARTICULAR SPRIFERMIN IN SYMPTOMATIC RADIOGRAPHIC KNEE OSTEOARTHRITIS: PRE-SPECIFIED ANALYSIS OF 3-YEAR DATA FROM A 5-YEAR RANDOMISED, PLACEBO-CONTROLLED, PHASE II STUDY

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Background: Sprifermin, a novel recombinant human fibroblast growth factor 18, is currently being investigated as a potential disease-modifying osteoarthritis (OA) drug. Two-year results of the 5 year phase II FORWARD study showed a statistically significant dose-dependent cartilage thickness increase in the total femorotibial joint (TFJ), and in the medial, lateral and central medial sub-region TFJ compartments by quantitative magnetic resonance imaging (qMRI).

Objectives: Here we report the pre-specified 3 year results.

Methods: Patients (pts) aged 40–85 years with symptomatic radiographic knee OA, Kellgren-Lawrence grade (KLG) 2 or 3, and medial mJSW ≥ 2.5 mm in the target knee were randomised (1:1:1:1) to receive 3 weekly i.a. injections with double-blinded placebo (PBO) or sprifermin, administered q6mo (0, 6, 12, and 18 months) or q12mo (0 and 12 months). The primary endpoint was the change in TFJ cartilage thickness from baseline (BL) to Year 2 with pre-specified analyses at Year 3. The intent-to-treat (ITT) population (all randomised pts) was used for non-qMRI endpoints; and the modified ITT population (all ITT pts with BL and ≥ 1 post-treatment MRI up to Year 2) for qMRI endpoints.

Results: 549 pts were randomised (median age 65 years, 69% women, 80% white, 69% KLG2, and ~70% predominantly medial disease); of which 18.4% (sprifermin) and 24.1% (PBO) discontinued the study within 3 years. TFJ cartilage thickness decreased from Year 2 to 3 in all treatment groups; however, the 0.05 mm difference between sprifermin 100 μ g q6mo and PBO was maintained (0.00 vs –0.05 mm; $p < 0.001$; figure 1a). Additionally, significant differences in mean cartilage thickness change from BL to Year 2 were maintained up to Year 3 with sprifermin 100 μ g vs PBO in both the medial (100 μ g q6mo –0.01 vs –0.06 mm; $p = 0.025$) and lateral TFJ compartments (100 μ g q6mo and q12mo: +0.01 and 0.00 vs –0.04 mm; $p < 0.001$ and $p = 0.003$, respectively), and central medial (100 μ g q6mo: +0.009 vs –0.084 mm; $p = 0.008$; figure 1b) and central lateral (100 μ g q6 and q12mo: +0.038 and +0.017 vs –0.053 mm; $p < 0.001$ and $p = 0.003$, respectively) TFJ sub-regions. The significant mean change from BL to Year 2 in lateral (but not medial) mJSW by X-ray was maintained up to Year 3 with both sprifermin 100 μ g groups vs PBO (100 μ g q6 and q12mo: +0.13 and +0.10 vs –0.11 mm; $p = 0.014$ and $p = 0.040$, respectively). By Year 2 total WOMAC scores were improved by ~50% in all treatment groups including PBO, and maintained up to Year 3 (18 months after last injection) without a significant difference between treatment groups. AEs and serious AEs remained balanced between groups at Years 2 and 3.

Abstract OP0059 – Figure 1 Mean change from baseline in cartilage thickness (by qMRI) over 3 years in: a) and b)

Conclusions: The 3 year results of the FORWARD study are consistent with the 2 year results: although cartilage thickness declined in all treatment groups between Year 2 and 3, the difference at Year 2 with sprifermin 100 µg vs PBO was maintained up to Year 3. Based on qMRI sprifermin is effective at increasing cartilage thickness in a dose-dependent manner in knee OA patients, and has an acceptable safety profile.

Disclosure of Interest: M. Hochberg Consultant for: Bioiberica SA, Bristol Myers Squibb, EMD Serono, Inc., Galapagos, IBSA Biotechniq SA, Novartis Pharma AG, Pfizer Inc., Plexikon, Samumed LLC, Theralogix LLC and TissueGene Inc., A. Guermazi Consultant for: OrthoTrophix, GE Healthcare, Merck Serono, AstraZeneca, Sanofi, TissueGene and Pfizer, Employee of: Boston Imaging Core Lab, LLC, H. Guehring Employee of: Merck KGaA, A. Aydemir Employee of: EMD Serono, Inc., S. Wax Employee of: EMD Serono, Inc., P. Fleuranceau-Morel Employee of: EMD Serono, Inc., A. Reinstrup Bihlet Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, I. Byrjalsen Employee of: Nordic Bioscience, J. Ragnar Andersen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, F. Eckstein Shareholder of: Chondrometrics GmbH, Consultant for: Merck KGaA, Samumed LLC, Abbvie, Bioclinica, TissueGene, Servier and Roche, Employee of: Chondrometrics GmbH

DOI: 10.1136/annrheumdis-2018-eular.2181

OP0060 KNEE JOINT DISTRACTION COMPARED WITH HIGH TIBIAL OSTEOTOMY AND TOTAL KNEE ARTHROPLASTY: TWO-YEAR CLINICAL, STRUCTURAL, AND BIOMARKER OUTCOMES

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Background: Knee joint distraction (KJD) is a new joint-preserving surgery technique that, like high tibial osteotomy (HTO), aims to delay total knee arthroplasty (TKA) especially in younger patients with knee osteoarthritis (OA). One year after treatment, KJD demonstrated similar beneficial outcomes compared to HTO and compared to TKA.^{1,2}

Objectives: To compare radiographic joint space width and clinical outcome over two-years for KJD vs TKA and for KJD vs HTO and to additionally study KJD cartilage repair by evaluation of systemic collagen type II markers.

Methods: End-stage knee OA patients considered for TKA were randomised to KJD (n=20; KJD_{TKA}) or TKA (n=40). Medial compartmental knee OA patients with a varus deviation of <10° considered for opening wedge HTO were randomised to KJD (n=23; KJD_{HTO}) or HTO (n=46). Distraction surgery was performed by use of

two external fixators with built in springs, placed lateral and medial of the knee joint. The knee was distracted 5 mm for 6 weeks and weight-bearing was encouraged.

WOMAC questionnaires (100 best) and VAS pain scores (0 best) were assessed at baseline (0), 3, 6, 12, 18 and 24 months. In the KJD groups, serum PIIANP and urine CTXII levels, as markers for collagen type II synthesis and breakdown, were determined over time. Normalised Z-indexes were calculated ($Z_{\text{index}} = Z_{\text{PIIANP}} - Z_{\text{CTXII}}$) to express net collagen type II synthesis. The minimum and mean joint space width (JSW) of the most affected compartment (MAC) were measured with KIDA software on standardised radiographs taken at 0, 12 and 24 months.

Results: Of the 129 included patients, 1, 6, 3, and 5 patients were lost in the KJD_{TKA}, TKA, KJD_{HTO}, and HTO group respectively, for various reasons. One-year structural and clinical outcomes were statistically significantly improved as reported before, and these beneficial effects sustained for at least two years after treatment when compared to baseline (figure 1A-C).

At 24 months, there were no significant differences between the KJD_{HTO} and HTO groups (all p>0.25) and between the KJD_{TKA} and TKA group, except for VAS pain score in favour of TKA at 24 months (p=0.037; figure 1B).

Compared to baseline, the ratio of synthesis over breakdown of collagen type II biomarkers (figure 1D) was significantly decreased at 3 months (-0.45 ± 0.20 ; p=0.032) after which this reversed towards an increase over time (at 24 months $+0.59 \pm 0.19$; p=0.004).

Abstract OP0060 – Figure 1 Change in A) total WOMAC score and B) VAS pain score after treatment with knee joint distraction (KJD), total knee arthroplasty (TKA) and high tibial osteotomy (HTO). KJD patients are divided in KJD_{TKA} (from the trial including patients for KJD and TKA) and KJD_{HTO} (from the trial including patients for HTO and TKA). C) change in minimum joint space width (JSW) measured on radiographs after KJD and HTO. D) change in biomarker Z-index changes for all KJD patients (KJD_{TKA} and KJD_{HTO} combined) after treatment. $Z_{\text{index}} = Z_{\text{PIIANP}} - Z_{\text{CTXII}}$, where the Z-values for both biomarkers are relative to baseline and (*) indicates statistically significant changes compared to baseline. In all graphs, the mean values $\pm$ SEM are given.

Conclusions: Sustained improvement of clinical benefit and increase in JSW after KJD is demonstrated for over 2 years of follow-up in case of treatment of patients with medial compartmental knee OA indicated for HTO or patients with end-stage knee OA indicated for TKA. The structural cartilage repair observed on radiographs is supported by a beneficial change in systemic biomarkers for collagen type II. For the HTO-indicated population, results of KJD patients were similar to those of HTO. For the TKA-indicated patients, TKA appeared to result in a slightly better clinical outcome, however at the expense of the native knee joint.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5846

OP0061 TREATMENT OF KNEE OSTEOARTHRITIS WITH SM04690 IMPROVED WOMAC A1 'PAIN ON WALKING' – RESULTS FROM A 52 WEEK, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, INTRA-ARTICULAR, WNT PATHWAY INHIBITOR

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Background: Knee osteoarthritis (OA) is characterised by pain, disability and joint deformity due to articular cartilage degradation and bone remodelling. Wnt