Objectives: To determine the role of inflammatory biomarkers at 2 years after anterior cruciate ligament (ACL) injury for predicting radiographic and magnetic resonance imaging (MRI)-defined knee OA 5 years post injury. Secondary aim was to estimate the concordance of inflammatory biomarkers assessed by MRI and in synovial fluid.

Methods: We studied 113 patients with acute ACL injury. 1.5 Tesla knee MRIs were read for Hoffa- and effusion-synovitis. Biomarkers of inflammation included IL-6, IL-8, IL-10, TNF- α and IFN- γ in serum and synovial fluid, and IL-12p70 in serum. The outcome was radiographic knee OA (ROA) or MRI-defined OA (MROA) at 5 years. Area under receiver operating characteristic curve (AUC), sensitivity and specificity were evaluated in models including MRI features only (M1), inflammation biomarkers only (serum [M2a] – synovial [M2b]) or both MRI and serum [M3a] or synovial [M3b] markers. Linear regression was used for evaluating association between MRI and synovial biomarkers.

Results: At 5 years, ROA was present in 26% and MROA was present in 32% of patients' injured knee. The AUCs (95% CI) for ROA were 0.44 (0.42–0.47;M1), 0.62 (0.59–0.65;M2a), 0.58 (0.55–0.61;M2b), 0.53 (0.50–0.56;M3a) and 0.50 (0.46–0.53;M3b) for each model. The corresponding AUCs for MROA were 0.67 (0.64–0.70), 0.49 (0.47–0.52), 0.65 (0.61–0.68), 0.56 (0.52–0.59) and 0.69 (0.66–0.72) (table 1). The associations between MRI and synovial biomarkers were weak and not statistically significant, apart from effusion-synovitis and IL-8 (log 10 IL8 levels were 0.23 and 0.43 higher in persons with grade 1 or 2/3, respectively).

Abstract OP0056 – Table 1 Discriminatory accuracy of imaging and serum/synovial fluid biomarkers at 2 years with respect to knee osteoarthritis (OA) development at 5 year according to 4 definitions using logistic regression model maximising area under receiver operating characteristic curve (AUC)

Outcome at 5 years	MRI features only (Model 1)	Serum biomarkers only (Model 2a)	MRI and serum biomarkers (Model 3a)	Synovial biomarkers only (Model 2b)	MRI and synovial biomarkers (Model 3b)
MRI OA					
AUC	0.67 (0.64; 0.70)	0.49 (0.47; 0.52)	0.65 (0.61; 0.68)	0.56 (0.52; 0.59)	0.69 (0.66; 0.72)
Sens	0.03 (0.01; 0.05)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)	0.02 (0.00; 0.03)	0.02 (0.00; 0.03)
Spec	0.99 (0.97; 1.00)	1.00 (1.00; 1.00)	1.00 (0.99; 1.00)	0.98 (0.96; 1.00)	0.99 (0.98; 1.00)
ROA					
AUC	0.44 (0.42; 0.47)	0.62 (0.59; 0.65)	0.58 (0.55; 0.61)	0.53 (0.50; 0.56)	0.50 (0.46; 0.53)
Sens	0.00 (0.00; 0.00)	0.01 (0.00; 0.03)	0.01 (0.00; 0.02)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Spec	1.00 (1.00; 1.00)	1.00 (1.00; 1.00)	1.00 (1.00; 1.00)	1.00 (1.00; 1.00)	1.00 (1.00; 1.00)
TF OA					
AUC	0.68 (0.65; 0.71)	0.52 (0.50; 0.54)	0.64 (0.62; 0.67)	0.53 (0.49; 0.56)	0.64 (0.60; 0.68)
Sens	0.22 (0.18; 0.26)	0.00 (0.00; 0.01)	0.13 (0.10; 0.17)	0.02 (0.00; 0.04)	0.14 (0.10; 0.19)
Spec	0.89 (0.88; 0.93)	0.99 (0.98; 1.00)	0.91 (0.89; 0.95)	0.95 (0.92; 0.98)	0.87 (0.84; 0.91)
PF OA					
AUC	0.62 (0.59; 0.65)	0.64 (0.61; 0.67)	0.65 (0.63; 0.68)	0.69 (0.65; 0.73)	0.68 (0.64; 0.73)
Sens	0.00 (0.00; 0.00)	0.22 (0.17; 0.28)	0.03 (0.01; 0.06)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Spec	1.00 (1.00; 1.00)	0.93 (0.91; 0.94)	0.99 (0.99; 1.00)	1.00 (1.00; 1.00)	1.00 (1.00; 1.00)

ROA= radiographic OA; TF=tibiofemoral; PFF=patellofemoral, AUC = area under the receiver operating characteristic curve

Conclusions: Neither MRI-defined inflammation, nor synovial/serum inflammation biomarkers at 2 years as analysed here predicted ROA or MROA at 5 years. The concordance between MRI and synovial inflammatory biomarkers was weak. Additional studies with longer follow-up will be needed to confirm or refute our findings and to more firmly define the role of inflammation for OA development following acute ACL injury.

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Acknowledgements: We thank the participants of the KANON study without this work would not have been possible.

Disclosure of Interest: F. Roemer Shareholder of: Boston Imaging Core Lab (BICL), LLC., M. Englund: None declared, A. Turkiewicz: None declared, A. Struglics: None declared, A. Guermazi Shareholder of: Boston Imaging Core Lab (BICL), LLC., Consultant for: Sanofi-Aventis, Merck Serono, OrthoTrophix, AstraZeneca, Pfizer, GE, and TissuGene, L. S. Lohmander: None declared, S. Larsson: None declared, R. Frobell: None declared

DOI: 10.1136/annrheumdis-2018-eular.2060

OP0057

EFFICACY AND SAFETY OF A DISTRACTION-ROTATION KNEE BRACE (ODRA) IN MEDIAL KNEE OSTEOARTHRITIS – A PHASE III RANDOMISED CONTROLLED TRIAL (ERGONOMIE STUDY)

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Background: According to EULAR and OARS guidelines, evidence is inconclusive for the symptomatic benefits of an unloader knee brace in medial knee osteoarthritis (OA).

Objectives: The objective of this multicenter randomised controlled trial (RCT) (*ClinicalTrials Id. NCT02765685*) was to compare the efficacy and safety of the ODRA brace, a distraction-rotation custom-made knee brace versus usual care over one year in medial knee OA.

Methods: Patients with symptomatic medial knee OA (VAS pain scores at rest >40/100 for the medial compartment) and Kellgren-Lawrence (KL) grade II-IV were randomised in two groups: brace group (ODRA +usual care) vs usual care alone (UCA). Patients were followed up every two months for one year. Usual care consisted of all the pharmacological and non-pharmacological treatments used for the management of knee OA. The primary end-point was the difference of VAS-pain between M0 and M12. Secondary end-points included patient global assessment of disease severity (PGA) on VAS,% of patients reaching the PASS (VAS-pain <30/100) and MCII (delta VAS-pain >20/100) thresholds at M12, KOOS scores, OA-specific quality of life questionnaire (OAKHQOL), as well as drug intake. Safety and compliance were evaluated by recording side effects and average knee brace duration of wear, respectively.

Results: Overall 120 patients (57% women) from 7 centres were included. Their characteristics were the following: mean age 63.6±11.4 years; BMI 29.6±5.5 kg/m²; OA duration 5.8±6 years; 52% KL III; 21% KL IV. The VAS pain decrease was statistically higher in the ODRA group (from 61.9±17.4 (M0) to 38.8±25.3 (M12) than in the UCA group (54.9±18.2 to 45.5±23.8) in the intent to treat bivariate and multivariate analyses (delta VAS-pain: 13.1±4.9, p<0.01). At M12, ODRA patients experienced a significant higher improvement than the UCA patients for PGA, all KOOS domains and for 3 of 5 domains of OAKHQOL (Pain, Physical activities, Mental health). Patients reaching PASS threshold at M12 were 42% in ODRA group vs 27% in UCA group (OR=3.04; 95% CI: 1.11 to 8.30; p<0.05) and were 46% vs 28% for MCII respectively (OR=2.65, 95% CI: 1.01 to 6.96; p<0.05). The overall analgesic use decreased more frequently in the ODRA group at M12 than in the UCA group (32.7% vs 15.4%, p<0.05) except for NSAIDs, HA or steroid injections. The compliance was good: the brace was worn for a median [IQR] duration of 5.7 [4.0–7.0] hours a day between M0 and M6 and 5.3 [3.7–6.3] hours a day between M6 and M12. Non-serious side effects were more common in the ODRA group (p<0.05) which justified the definitive withdrawal of the brace in 8 ODRA patients (13%), mainly for cutaneous side effects.

Conclusions: In this RCT, the use of the ODRA brace in addition to usual care was shown to be superior to usual care alone in reducing symptoms and improving quality of life of patients suffering from medial knee OA, with good compliance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4927

OP0058

LOW-DOSE RADIATION THERAPY AS TREATMENT FOR HAND AND KNEE OSTEOARTHRITIS: TWO DOUBLE-BLIND RCT'S

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Background: Synovial inflammation plays an important role in osteoarthritis (OA) pathophysiology. In some countries, low-dose radiation therapy (LD-RT) is widely used as treatment for OA, while relatively unknown in others. Studies *in vitro* and in OA animal models have shown anti-inflammatory effects of LD-RT. However, systematic literature review has shown that high-level evidence for beneficial effects in clinical practice is lacking.

Objectives: To assess the effect of LD-RT on clinical outcomes and inflammation in patients with hand or knee OA, using two parallel prospective RCTs.

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.