Table 1. Comparison of the disease activity measures reported by the physician and by the nurse.

	Physician	Nurse	p-value
Total Joint Count	4.87 (2.26)	5.02 (6.20)	0.152
Swollen Joint Count	2.13 (3.88)	2.15 (3.83)	0.790
Global Assessment	3.30 (2.41)	3.32 (2.43)	0.702
DAS-28	3.97 (1.52)	3.90 (1.54)	0.002
CDAI	14.26 (12.53)	14.38 (12.59)	0.515
SDAI	21.51 (23.57)	21.61 (21.66)	0.527

Figure 1. Agreement between physician- and nurse-DAS categories

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New drugs and therapies

POS0276

EFFICACY OF KRILL OIL IN THE TREATMENT OF KNEE OSTEOARTHRITIS: A 24-WEEK MULTICENTRE RANDOMISED DOUBLE-BLIND CONTROLLED TRIAL

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Background: Elevated levels of systemic inflammation are common in people with osteoarthritis and predict both pain and structural outcomes. Krill oil has anti-inflammatory properties and reduces severity of inflammatory arthritis in mice by 50% compared to controls.¹ In humans, krill oil reduced knee pain and function in two short, moderate quality randomised controlled trials (RCTs) in people with osteoarthritis. However, evidence from longer trials with imaging data is lacking.

Objectives: The aim of this study was to compare the efficacy of krill oil (2g / day) vs. placebo for treating knee pain in patient with clinical knee osteoarthritis who have significant knee pain and effusion-synovitis.

Methods: KARAOKE was a 24-week multicentre, randomised, double-blind, placebo-controlled trial conducted at five Australian sites. Participants aged ≥40 years with symptomatic knee OA (according to ACR criteria), significant knee pain (pain score ≥40mm on a 100mm visual analogue scale [VAS]), and effusion-synovitis present on MRI (grade ≥1 according to modified Whole-Organ Magnetic Resonance Imaging Score (WORMS) scoring) were eligible. The study protocol has been published previously.² Participants were randomised to receive 2g/day of krill oil, (350mg/g omega-3 content, 12mg/g total omega-6 content) or inert placebo (vegetable oil, no EPA or DHA, <5mg/g (0.05%) other omega-3s).

The primary outcome was absolute change in knee pain assessed using a VAS [0-100mm] after 24 weeks. Secondary outcomes were: change in knee pain and function assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score [0-500mm]), change in back and hand pain assessed using a VAS [0-100mm], change in lower limb leg strength assessed using a dynamometer, and change in blood parameters (including CRP, triglycerides, fasting glucose and total, HDL, LDL cholesterol), after 24 weeks.

Linear mixed-models were used, using patient identification as random intercepts and trial centre and treatment month as random effect to adjust for correlated data within trial centres and repeated measures and to allow different treatment effects among patients over time, respectively.

Results: 262 participants were randomised (mean age 61.5 years, 53% females) to receive krill oil (n=130) or placebo (n=132). A total of 85% completed the trial. Knee pain improved in both groups over 24 weeks, but with no between-group difference (krill oil, -20.1mm; placebo, -19.3mm, p=0.81). Secondary outcomes: knee pain and function score improved in both groups, but with no between-group difference (WOMAC pain: krill oil, -86.7; placebo, -82.5mm, p=0.81; WOMAC function: krill oil, -245.3; placebo, -184.3, p=0.14 at 24 weeks). The same applies for hand pain and back pain. No significant changes were seen in leg strength or any of the blood parameters at 24 weeks). Incidence of one or more adverse events was 50% in the krill oil group (n=66) and 55% in the placebo group (n=71). There were 8 serious adverse events in the krill oil group 6 in the placebo group, all considered unrelated to treatment.

Conclusion: Krill oil was safe and well tolerated, but did not significantly reduce knee pain in patients with clinical knee osteoarthritis, significant knee pain and effusion-synovitis after 24 weeks compared to placebo. These findings do not support use of krill oil for alleviating knee pain in clinical knee osteoarthritis.

REFERENCES:

1. Ierna M, et al. BMC Musculoskelet Disord 2010;11:136.
2. Laslett L, et al. Trials 2020;21:79

Outcomes	Absolute between group difference at 24 weeks	P value
Primary		
Knee pain	0.8 (-5.6 to 7.2)	0.81
Secondary		
Knee pain (WOMAC)	4.2 (-29.1 to 37.5)	0.81
Knee function (WOMAC)	61 (-19.2 to 141.3)	0.14
Hand pain	2.8 (-2.6 to 8.3)	0.31
Back pain	1.9 (-3.9 to 7.8)	0.46
Leg strength	-2.59 (-9.41 to 4.23)	0.52
Metabolic factors		
Total Cholesterol	0.09 (-0.1 to 0.29)	0.34
HDL Cholesterol	-0.03 (-0.1 to 0.03)	0.35
LDL Cholesterol	0.05 (-0.12 to 0.22)	0.57
Triglycerides	0.12 (-0.09 to 0.33)	0.27
Fasting glucose	0.01 (-0.26 to 0.29)	0.93
hsCRP	0.64 (-0.56 to 1.84)	0.30

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POS0277

ANABOLIC EFFECT OF LNA043, A NOVEL DISEASE-MODIFYING OSTEOARTHRITIS DRUG CANDIDATE: RESULTS FROM AN IMAGING-BASED PROOF-OF-CONCEPT TRIAL IN PATIENTS WITH FOCAL ARTICULAR CARTILAGE LESIONS

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Background: LNA043 is a modified, recombinant version of the human angiopoietin-like 3 (ANGPTL3) protein acting directly on cartilage-resident cells to transmit its cartilage anabolic effect. A first-in-human study previously demonstrated the favourable safety profile and the modulation of several pathways involved in cartilage homeostasis and osteoarthritis (OA)¹. A previous proof-of-mechanism imaging study used high field (7 Tesla) magnetic resonance imaging (MRI) to show formation of hyaline-like tissue after a single injection of 20mg LNA043 (unpublished data).

Objectives: To evaluate non-invasively the chondro-regenerative capacity of multiple intra-articular (i.a.) injections of LNA043 in patients with articular cartilage lesions in the knee (NCT03275064).

Methods: This was a randomised, double-blind, placebo (PBO)-controlled, proof-of-concept study in patients with a partial thickness cartilage lesion. In total, 58 patients (43 [20mg LNA043]; 15 [PBO]), stratified by lesion type (condylar or patellar) were treated with 4 weekly i.a. injections. The primary endpoint was T2 relaxation time measurement as a marker of collagen fiber network, and cartilage lesion-volume was a secondary endpoint, both using 3-Tesla MRI. Assessments were performed at baseline, weeks (wks) 8, 16, 28 and 52 (the latter in 23/58 patients). While lesion-volume for the secondary endpoint was determined from manually segmented images, the cartilage volume of 21 sub-regions spanning the entire knee was also measured from 3D isotropic MR images employing an automated segmentation prototype software (MR Chondral Health 2.1 [MRCH], Siemens Healthcare)². An exploratory analysis evaluated the treatment effect for the additive volume of the 3 subregions in the weight-bearing area of the medial femur.

Results: No change in T2 relaxation time was detected between treatment and PBO groups. Manual segmentation showed continuous filling of the cartilage lesions up to wk 28 in LNA043-treated patients with femoral lesions ($p=0.08$, vs PBO) while no effect was detected for patients with patellar lesions. Given the limitations of measuring small, irregularly shaped lesions with manual image-analysis, the MRCH approach was used (Figure 1). In the medial femoral weight-bearing region, refilling was detected over time ($\Delta=123\text{mm}^3$ at wk 28, $N=37$, $p=0.05$). No overgrowth was detected in the lateral femoral condyles without cartilage damage. The overall safety profile was favourable; only mild/moderate local reactions were reported, including a higher incidence of joint swelling (9.3% vs 0%) and arthralgia (11.6% vs 6.7%) for LNA043 vs PBO resolving spontaneously or with paracetamol/NSAIDs. No anti-drug antibodies were detected.

Conclusion: Treatment with 4 weekly i.a. injections of 20mg LNA043 resulted in regeneration of damaged cartilage in patients with femoral articular cartilage lesions. Automated measurement of cartilage volume in the femoral index region was able to detect a relevant treatment effect and was found to be more sensitive than the manual segmentation method. No sign of cartilage overgrowth was observed in healthy femoral regions. A Phase 2b study in patients with mild to moderate knee OA is in preparation.

REFERENCES:

[1] Scotti et al. *ACR Convergence* 2020; Abstract #1483

[2] Juras et al. *Cartilage* 2020; Sep 29:1-12

Figure 1. Example of successful lesion filling from 3D reconstruction of cartilage MRI in an LNA043-treated patient with damage in the medial femur. Note the complex nature of the lesion which turns out to be deep in its center but shallower in the periphery. No scan is available for this patient at Week 52.

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POS0278

A MULTICENTER, OBSERVATIONAL, EXTENSION STUDY EVALUATING THE SAFETY, TOLERABILITY, AND EFFICACY OF A SINGLE LORECIVIVINT INJECTION IN KNEE OA SUBJECTS

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Background: Lorecivint (LOR), a novel intra-articular (IA) CLK2/DYRK1A inhibitor that modulates the Wnt pathway, is in development as a knee osteoarthritis (OA) treatment.

Objectives: Subjects from two consecutive Phase 2 trials were followed up in a 5-year, pooled, observational study that evaluated the safety and exploratory efficacy of a single LOR injection that was previously administered into the target knee joint of subjects with moderate to severe knee OA. The study was terminated in its third year, as relevant long-term safety information became limited in the absence of repeated LOR administration. The primary objective evaluated the incidence of serious adverse events (SAEs). Safety data for all doses and a post hoc efficacy analysis for the pivotal dose (0.07 mg LOR) are reported.

Methods: This was a Phase 3, multicenter, observational, extension study of completer subjects (OA-05; NCT02951026) from two Phase 2 trials of LOR: a 12-month Phase 2a trial (OA-02; NCT02536833)¹ and a 6-month Phase 2b trial (OA-04; NCT03122860)². Subjects received a single LOR or control (placebo or vehicle) injection at their parent-study baseline visit (OA-02 or OA-04 Visit 0 in this analysis). Pooled data from clinic visits at 6, 12, 24, and 36 months contributed to the extension-study (OA-05) analysis. SAEs, knee-related adverse events (AEs), and AEs of newly diagnosed conditions requiring treatment were collected as safety outcomes. Efficacy was assessed by target knee WOMAC Pain and Function subscores and radiographic medial joint space width (mJSW). A post hoc analysis was performed for 0.07 mg LOR versus control to assess responses in a subject subgroup (unilateral symptoms, no widespread pain, 18-month post-injection radiograph at study termination). Baseline-adjusted ANCOVA was performed using data from both the current and parent studies at 0, 3, 6, 12, and 18 months.

Results: Of 703 subjects, 119 (17%) subjects discontinued prior to study termination. Subjects had a mean age of 60.7 years and mean BMI of 29.1 kg/m², and 61% were female. The majority of subjects had KL 3 (61.2%) OA. The safety analysis set included 495 LOR-treated subjects and 208 control subjects.