months, the mean number of consultations with HCPs increased with disease severity (3.7 mild, 4.2 moderate and 5.7 severe [<0.001]). This pattern was also observed in relation to the mean number of tests/scans conducted in the last 12 months (6.9 mild, 7.9 moderate and 9.3 severe [<0.001]). More than a quarter of severe patients visited the ER in the last 12 months (26% vs. 4% mild; 9% moderate [<0.001]) and visits to hospital increased with disease severity (Table 1). The proportion of patients that have had a surgery due to their OA rose with worsening disease severity (11%, 13% and 27% for mild, moderate and severe, respectively [<0.001]).

Table 1. Physician-reported healthcare burden by OA disease severity

	Mild (n=874)	Moderate (n=1904)	Severe (n=818)
Number of patient visits to ER in the last 12 months, mean (SD)	0.1 (0.4)	0.1 (0.6)	0.5 (1.0)
Patients with ≥ 1 emergency visit in the last 12 months, n (%)	13 (1.5)	43 (2.3)	79 (9.7)
Patients with ≥ 1 hospitalisation in the last 12 months, n (%)	11 (0.1)	9 (0.5)	26 (3.2)
Number of patient outpatient hospital visits in the last 12 months, mean (SD)	0.5 (1.4)	0.6 (1.1)	1.2 (1.4)

Conclusion: This real-world data demonstrated an increase in visits to HCPs, monitoring tests and scans, hospitalisations, ER visits and surgery as OA disease severity worsened.

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FRI0398

COMPARISON OF THE EFFICACY AND SAFETY OF TWO HYALURONIC ACIDS IN THE TREATMENT OF KNEE OSTEOARTHRITIS

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Background: Several viscosupplement treatments are available to patients suffering from osteoarthritis (OA) but few comparative clinical trials have been conducted.

Objectives: The primary objective of the study was to demonstrate at 24 weeks the non-inferiority of on hyaluronic acid over a second one in terms of efficacy (pain relief) in knee OA patients (Kellgren and Lawrence radiologic stage II or III) with whom oral treatment had failed.

Methods: This was a prospective, multicenter, comparative, randomized, double-blinded study (one independent physician evaluator—one physician injector), comparing two viscosupplements: one containing a solution of hyaluronic acid (SYNOLIS VA® 80mg hyaluronic acid and 160mg sorbitol – Group HA1) and the other containing one of Hylan (SYNVISCO ONE® 48mg Hylane GF-20 – Group HA2) over a period of 24 weeks. At inclusion, the average VAS Pain (1-100) was 62.5. The patients were randomized in 2 parallel groups at D0 and followed until D168. They received an injection of either HA1 or HA2. Efficacy was primarily assessed using the WOMAC Pain index (daily assessed by the patient during seven days following the injection, and then at D14). During the follow up visits (D28-D84-D168) WOMAC pain, stiffness and function scores were assessed as secondary objectives. At D168, efficacy and satisfaction were also evaluated by the evaluator and by the patient using Likert scale (7 points). Moreover, the number of responders strict each group was evaluated according to the OMER-ACT-OARSI criteria. According to methodology guidelines, the per protocol (PP) population has been used as primary analysis. The PP population included all patients from the intention to treat (ITT) population who completed the study without any major protocol violation.

Results: 202 patients were randomized (ITT population, 96 in the HA1 group and 106 in the HA2 group). Baseline demographic data for the PP population at the time of randomization by treatment group. Patients were predominantly female (66%). The median age of the whole population was 65 years and the median body mass index of 27.4 kg/m². No statistically significant differences between the two treatment groups were observed for any demographic criteria. At D168, 197 presented no protocol violations (94 in the HA1 group and 103 in the HA2 group). This population had a decrease on the overall score of the WOMAC Pain at -29.2 +/- 24.1 (SD) in the HA1 group and -31.6 +/- 25.5 (SD) in the HA2 group confirming the non-inferiority ($P = 0.57$ for the difference between groups). Regarding the secondary endpoints, no significant difference has been observed at D14, D28, D84, D168, in the PP population for all the outcome except stiffness at D28. There was also no difference between the responders rate in two groups (79 % for HA1 and 77% for HA2). In terms of safety, both products were well tolerated. No case of allergy or infection in the course of the injection was reported. Serious adverse events have been reported by 4 patients in HA1 group and 3 in HA2 group.

Conclusion: In this study, we confirmed the non-inferiority of HA1 compared with HA2 in terms of both efficacy and safety.

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FRI0399

COLCHICINE IS NOT EFFECTIVE FOR REDUCING OSTEOARTHRITIC HAND PAIN COMPARED TO PLACEBO: A RANDOMISED, PLACEBO-CONTROLLED TRIAL (COLAH)

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Background: Current pharmacotherapies to treat or prevent hand osteoarthritis are limited. Colchicine, an anti-inflammatory agent effective at reducing joint pain and swelling in gouty arthritis, may offer relief in hand osteoarthritis, though this has not been investigated before.¹

Objectives: To investigate the efficacy of colchicine compared to placebo on VAS pain scores over 12 weeks in adults with hand osteoarthritis in a randomised, double-blind controlled trial.

Methods: 64 community-dwelling adults with hand osteoarthritis (American College of Rheumatology criteria)² (54 females, 48-79 years) were randomised 1:1 to colchicine (0.5mg twice daily) or placebo for 12 weeks. VAS pain scores (worst affected hand) were obtained at baseline and weeks 6, 12, and after treatment withdrawal at week 16. Secondary outcome measures included grip strength, C-reactive protein (CRP) and tender and swollen joint count (TSJC). Grip strength, TSJC and CRP were obtained at baseline and week 12. Intention-to-treat analyses, adjusted for age and gender, were performed using constrained longitudinal data analysis models in Stata v16.³ This study is registered with the Australia New Zealand Clinical Trials Registry, ACTRN12617001524381.

Results: 58 participants completed the study (N=27 colchicine, N=31 placebo, withdrawal rate 9%). Mean (S.D.) VAS score of the affected hand at baseline was 71.4 (14.5) mm in the placebo and 65.4 (15.0) mm in the colchicine group ($p = 0.11$). VAS scores improved during treatment, but were comparable between groups at week 6, 12 and 16 (Table 1). There were no differences between groups at week 12 for CRP, TSJC or grip strength (Table 1). Adverse events related to study medications included nausea (n=4), diarrhoea (n=9), vomiting (n=3), bloating (n=1) and reflux (n=1).

Table 1. COLAH study primary and secondary outcomes, from constrained longitudinal data analysis model

Outcome	Timepoint	Colchicine (SE)	Placebo (SE)	Colchicine-Placebo (95% CI)	p-value
VAS Pain (mm)	6 weeks	53.5 (4.5)	53.9 (4.6)	-0.4 (-12.3, 13.1)	0.95
	12 weeks	57.1 (4.4)	48.4 (4.6)	8.7 (-21.2, 3.9)	0.18
	16 weeks	62.0 (4.3)	61.6 (3.7)	-0.4 (-11.4, 10.5)	0.94
TSJC (0-20)	12 weeks	5.6 (0.7)	3.8 (0.7)	1.8 (-4.1, 0.5)	0.13
Grip strength (kg)	12 weeks	14.4 (0.8)	15.3 (0.8)	-0.9 (-0.2, 2.0)	0.10
CRP (mg/L)	12 weeks	4.5 (1.4)	4.0 (1.3)	0.5 (-3.8, 2.9)	0.77

Conclusion: Colchicine 1mg daily for 12 weeks was not effective in improving pain, tender and swollen joint count or grip strength in symptomatic hand osteoarthritis patients. This study does not support colchicine for treatment of symptoms of hand osteoarthritis.

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FRI0400

EFFICACY AND SAFETY OF AN INTRA-ARTICULAR INJECTION OF JTA-004, A NOVEL ENHANCED PROTEIN SOLUTION, IN KNEE OSTEOARTHRITIS PAIN: A RANDOMISED, DOUBLE-BLIND CONTROLLED PHASE II/III STUDY

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Background: Osteoarthritis (OA) is a degenerative, chronic, and progressive joint disease. It is associated with chronic pain, joint function impairments and disabilities, causing a poorer quality of life with physical and/or mental co-morbidity. Along with population ageing and increasing obesity, the incidence of OA is rising and there is an urgent need for new treatment options.

Objectives: JTA-004 is a novel protein solution in development for the treatment of knee OA pain. Supplemented with hyaluronic acid and clonidine, it is designed to provide a fast-acting and long-lasting pain relief. To evaluate efficacy and safety and to select the most effective formulation, single intra-articular administration of 3 JTA-004 formulations were tested and compared to Hylan G-F 20 during a 6-month period.

Methods: In this prospective, multicentre, double-blind phase II/III trial (NCT02740231), eligible participants were 50-79-year-old men and women with primary knee OA classified with Kellgren-Lawrence grade II or III and a body mass index (BMI) under 35. 164 patients were randomly assigned to one of the three JTA-004 formulations or the reference treatment (Hylan G-F 20) in a 1:1:1:1 ratio. The three JTA-004 formulations differed in their clonidine concentration (50 or 100 µg/ml) and/or their volume of injection (2 or 4 ml) (Table 1). Patients were evaluated using Western Ontario McMaster Universities (WOMAC®) scores and Short-Form health survey (SF-12). The primary efficacy endpoint was the change from baseline at 6 months in WOMAC® VA3.1 Pain Subscale. Safety was assessed by monitoring and reporting vital signs, physical examination, adverse events and concomitant medications throughout the study.

Table 1. Description of the three JTA-004 formulations administered

JTA-004 formulation	Plasma protein solution		Clonidine		HA		Volume of	
	Concentration	Amount	Concentration	Amount	Concentration	Amount	injection	
JTA-100/2	1.02 g/ml	2.04 g	50 µg/ml	100 µg	10 mg/ml	20 mg	2 ml	
JTA-200/2	1.02 g/ml	2.04 g	100 µg/ml	200 µg	10 mg/ml	20 mg	2 ml	
JTA-200/4	1.02 g/ml	4.08 g	50 µg/ml	200 µg	10 mg/ml	40 mg	4 ml	

Results: At 6 months, patients in the three JTA-004 groups showed a better improvement in pain compared to patients in the reference group. The between-group difference (between each JTA-004 test group and reference group) in adjusted (adapted to difference in baseline values) mean change in WOMAC® Pain Subscale Score from baseline ranged between -9.49 mm and -11.63 mm at 6 months post-injection. Statistical superiority of each JTA-004 formulation over Hylan G-F 20 was however not demonstrated (p-value between 0.052 and 0.141) (Figure 1, JTA 200/2, 100/2 and 200/4). As the three JTA-004 formulations had a similar efficacy in terms of pain reduction, a *post hoc* analysis was subsequently performed between the pooled JTA-004-treated patients and the reference group. This analysis showed a 26.1 ± 2.4 (adjusted mean $\pm$ SE) mm improvement in pain in the pooled JTA-004 group vs. 15.6 ± 4.1 mm in the reference group at 6 months, demonstrating a statistically significant superiority of JTA-004 over the reference (between-group difference = -10.57; p = 0.030) (Figure 1, pooled JTA).

Figure 1. Main and post hoc analyses.

All JTA-004 formulations were shown to be well tolerated and had a clinically acceptable safety profile. There was a trend for fewer treatment-related events in the JTA-100/2 group, notably no cases of post-injection mild and transient hypotension.

Conclusion: This study provides a first evidence of efficacy and safety of JTA-004 in the treatment of knee OA pain.

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