There were 169 AEs reported by 110 [15.6%] subjects. Four AEs were considered to be related to study drug and were reported by 3 (0.6%) subjects across LOR groups; no subjects withdrew from the study due to a treatment-related AE. The most common AEs were osteoarthritis (28 [4.0%] subjects) and arthralgia (25 [3.6%] subjects); incidence was similar between LOR and control groups. During the study, 68 SAEs were reported by 38 (5.4%) subjects, and no SAEs were considered to be related to treatment by investigator. One death occurred in the control group. Post hoc efficacy analyses demonstrated that subjects in the 0.07 mg LOR group (n=59) showed greater improvements from baseline in both WOMAC Pain and Function at 6 and 12 months versus subjects in the control group (n=70) (Figure 1; Day 0):

6 months:Pain: -8.16, 95% CI [-15.60, -0.71], $P=0.032$

Function: -9.47, 95% CI [-17.09, -1.84], $P=0.015$

12 months:Pain: -8.51, 95% CI [-15.17, -1.85], $P=0.013$

Function: -9.62, 95% CI [-16.83, -2.42], $P=0.009$

No mJSW progression was observed in any group over 18 months.

Limitations to this analysis include 1) subjects from LOR and control groups were "completers," therefore, more likely to be responders, and 2) subjects could have been on any medication or treatment in the extension study.

Conclusion: From these data, LOR appeared to be safe and well tolerated. A post hoc-analyzed subset of completer subjects treated with a single 0.07 mg LOR injection reported durable symptom improvements in WOMAC Pain and Function for up to at least 12 months versus control subjects.

*Pooled data from the OA-02, OA-04, and extension study; includes all available data from 3, 6, 12, and 18 months after injection. * $P<0.05$, ** $P<0.01$

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Disclosure of Interests: Ismail Simsek Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Heli Ghandehari Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Nebojsa Skrepnik Consultant of: Pfizer, Regeneron, Orthofix, Grant/research support from: Samumed, LLC
DOI: 10.1136/annrheumdis-2021-eular.2240

POS0279

WEARABLE TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION DEMONSTRATED BETTER EFFICACY AND SAFETY THAN WEAK OPIOIDS IN THE TREATMENT OF MODERATE TO SEVERE, CHRONIC NOCICEPTIVE PAIN IN KNEE OSTEOARTHRITIS. A RANDOMIZED, CONTROLLED, NON-INFERIORITY TRIAL

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Background: In knee osteoarthritis (KOA) recommendations, the first pharmacological analgesic line is paracetamol. However, its low efficacy, frequently leads to the use of weak opioids (WO) despite their poor tolerance, especially in elderly patients. **Objectives:** The primary objective was to compare analgesic efficacy and safety of a new wearable transcutaneous electrical nerve stimulation (W-TENS) to those of WO in the treatment of moderate to severe, nociceptive, chronic pain in KOA patients.

Methods: ArthroTENS study was a phase 3, non-inferiority, multicentric, prospective, randomized, single-blinded for primary efficacy outcome, controlled, in 2-parallel groups, clinical study comparing W-TENS versus WO on two periods: a 3-month controlled period and an additional, optional, non-controlled, 3-month follow-up for patients in W-TENS group.

Eligible participants were KOA patients, ≥ 55 years old, at Kellgren-Lawrence radiographic grade ≥ 2 , with moderate to severe nociceptive chronic (≥ 3 months) mean 8-day pain ≥ 4 on a 11-point numerical rating scale, and in treatment failure with non-opioid analgesics, including NSAIDs. Patients with neuropathic pain were excluded.

Co-primary endpoints were, for efficacy, mean pain intensity (PI), assessed at M3 and, for safety, the number of adverse events (AE) during the 3-month follow-up period.

In W-TENS group, an advanced, mobile app enabled, wearable TENS was used. High (100 Hz) and low (2 Hz) frequency stimulations were delivered via electrodes with standardized positioning (Figure 1).

Figure 1. Electrode's positioning

In WO group, investigators chose, for each patient, the best suitable WO and its daily dose, and could switch to another WO, and/or adapt its daily dose if necessary.

A non-inferiority analysis was performed on the primary efficacy endpoint using a pre-defined non-inferiority margin (0.825 point) on PI, below the minimal clinically significant improvement.

Results: Demographic and baseline characteristics were balanced across both groups.

110 patients (55/group) were randomized and 48/55 (87.3%) and 44/55 (80.0%) patients completed the 3-month follow-up in W-TENS and WO groups, respectively. WO's prescriptions were balanced between codeine, opium-powder, tramadol and WO-paracetamol combinations.

Non-inferiority of W-TENS was demonstrated in the PP and ITT populations (Table 1). Since the 95% confidence interval (CI) of the between-treatments difference was below 0 in the ITT population, a planned superiority analysis was performed showing that W-TENS was significantly superior to WO at M3 ($p=0.0124$) on PI. Additionally, the number of AEs was significantly lower ($p<0.001$) in W-TENS (n=7) group than in WO (n=36) group. In WO group, AEs were systemic AEs usually reported with WO while AEs in W-TENS group were local, related to the technique used, such as local cutaneous reaction (erythema).

Table 1. Non-inferiority analyses on pain intensity at M3. ITT and PP populations. Least squares means for each study group and study group difference estimate and corresponding 95% CI

Group Population	Within-group change		Between-group difference	
	W-TENS	WO	W-TENS - WO	
ITT Population (n)	55	55		
Non inferiority				
Mean (SD)	3.83 (0.28)	4.74 (0.28)	-0.92 (0.40)	Non inferiority†
95% CI	[3.27, 4.40]	[4.18, 5.30]	[-1.71, -0.12]	demonstrated
PP Population (n)	52	47		
Mean (SD)	3.87 (0.30)	4.66 (0.32)	-0.79 (0.44)	Non inferiority†
95% CI	[3.28, 4.46]	[4.03, 5.28]	[-1.65, 0.08]	demonstrated

† Noninferiority was demonstrated when 95% CI < 0.825

Thirty-nine (70.9%) patients wished to extend W-TENS treatment for 3 additional months. Only one patient discontinued this additional period and results obtained at M3 remained stable at M6.

Conclusion: In this study, W-TENS was more effective and better tolerated than WO in the treatment of nociceptive KOA chronic pain and should represent an interesting non-pharmacological alternative to WO.

Acknowledgements: We gratefully thank P. Fardellone (Amiens), E. Coudreyre (Clermont-Ferrand), Y. Donazzolo (Gieres), A. Amouzougan (Saint-Etienne), L. Grange (Grenoble), T. Conrozier (Belfort), E. Senbel (Marseille), J.P. Sanchez (Billere), R. Forestier (Aix-les-Bains), H. Bard (Paris) and E. Gibert (Ivry-sur-Seine) for their active contribution throughout arthroTENS study

Disclosure of Interests: Emmanuel Maheu Speakers bureau: TRB chemedica, Consultant of: SUBLIMED, Moirans, FRANCE; Sandrine Soriot-Thomas Speakers bureau: Grunenthal, Consultant of: SUBLIMED, Moirans, FRANCE;

Grunenthal

Kyowa Kirin pharma, Grant/research support from: Grunenthal

Sanofi

Teva

Mylan

Therable, Eric Noel Consultant of: SUBLIMED, Moirans, FRANCE; Eric Lespes-sailles Consultant of: SUBLIMED, Moirans, FRANCE; Bernard Cortet Consultant of: SUBLIMED, Moirans, FRANCE;

DOI: 10.1136/annrheumdis-2021-eular.2086

POS0280

ASSOCIATION OF COMPLEMENTARY AND ALTERNATIVE MEDICINE USE WITH KNEE SYMPTOMS AND KNEE STRUCTURAL CHANGES OVER 2.6 YEARS: A POPULATION-BASED COHORT STUDY OF TASMANIAN OLDER ADULTS

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Background: There is increasing use of complementary and alternative medicines (CAMs) alone or as an adjuvant therapy to conventional palliative medicines.¹ However, there remains clinical uncertainty about the benefit of CAMs in the management of osteoarthritis in older population.

Objectives: To describe the association between CAM use (alone or in combination with conventional analgesics) with knee symptoms and structural changes amongst a representative sample of Tasmanian older adults.

Methods: A total of 1,099 participants were selected from the Tasmania Older Adult Cohort Study (TASOAC), an ongoing prospective population-based study. Exposure to CAM and conventional medications was classified into four categories according to the national drug code directory: ² CAM only, conventional analgesics only, both CAM and conventional analgesics, and neither CAMs nor conventional analgesics. Knee pain was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and a 1.5-T MRI of the right knee was performed at baseline and follow-up (around 2.6 years). Longitudinal associations were assessed using mixed effect linear models.

Results: At baseline, participants' mean age was 63, 86.5% (n=951) reported any medication use. The prevalence of CAM use was 35.0% and of conventional analgesics was 58.6%. Over follow-up, the analgesic only group had a significant increase in WOMAC pain, function, and stiffness scores compared to those who took neither CAMs nor conventional analgesics. There was a statistically significant femoral cartilage volume loss across all four groups, and no statistical difference was found between participants who takes both CAMs and analgesics group and the reference group, but participant in the CAM only or the analgesics only groups loss statistically significant more femoral cartilage volume than the reference group (Table 1).

Conclusion: CAM use alone or in combination with conventional analgesics may associate with slower progression of knee pain. Conclusive evidence on the longitudinal benefits of CAM in the management of osteoarthritis among older adults warrants more studies.

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Table 1. Association of change in clinical knee symptoms and knee structural changes over 2.6 years with different medications groups.

	Mean change for reference group*	Change for each category, coefficient (95% confident intervals)			Reference group*
		CAMs	Both	Analgesics	
No. of participants	327	128	257	387	327
WOMAC	-0.95	0.04	0.32	0.78	Ref
pain (5-50)	(-1.42, -0.48)	(-0.85, 0.93)	(-0.4, 1.04)	(0.13, 1.43)	
WOMAC function (17-170)	-3.09	1.02	1.39	2.32	Ref
	(-4.52, -1.67)	(-1.7, 3.73)	(-0.81, 3.59)	(0.33, 4.31)	
WOMAC stiffness (2-20)	-0.39	0.15	0.35 (0, 0.7)	0.40	Ref
	(-0.62, -0.17)	(-0.28, 0.58)		(0.09, 0.72)	
Femoral cartilage volume (mL)	-187.98	-113.81	-1.92	-127.19	Ref
	(-228.79, -147.18)	(-192.60, -35.03)	(-65.00, 61.17)	(-186.31, -68.06)	

*Reference group=participants taken neither CAMs nor conventional analgesics

The data were fitted using mixed effect linear models, which were constructed by entering baseline medication group, phase, the interaction between medication group and phase, covariates (baseline age, sex, body mass index [BMI], baseline value of outcome), the interaction between the covariates and phase, random intercept, and random slope on phase (time).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2762

POS0281

RUBUS IDAEUS LEAF EXTRACT IMPROVES SYMPTOMS IN KNEE OSTEOARTHRITIS PATIENTS: RESULTS FROM A DOUBLE BLIND RANDOMIZED CLINICAL STUDY

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Background: Osteoarthritis (OA) is the most common cause of disability in older adults. Currently, the aim of the patient management is to reduce symptoms and to improve quality of life using therapeutic modalities with no adverse effects (1). Unfortunately, the first line treatments of OA symptoms remain nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol which if long-term administration are associated with severe adverse effects. Therefore, we need of save alternative to manage chronic OA symptoms. One candidate is *Rubus idaeus* (raspberry) leaf extract rich in flavonoids and phenols known to inhibit inflammatory responses.

Objectives: The aim of this study was to investigate the effects of a 12-weeks intervention with an ethanolic extract from *Rubus idaeus* leaf on symptoms of knee OA.

Methods: The study was a randomized, double-blind, placebo-controlled, monocentric trial of 198 subjects with femoro-tibial OA. Subjects were randomized equally to receive one daily treatment during 3 months either of 1 cap of *Rubus idaeus* leaf extract 400mg, or 200mg or placebo (maltodextrine). The main objective of this first exploratory study was to assess pain reduction over time. Pain was measured using different scales from the Western Ontario McMaster osteoarthritis index (WOMAC) to the knee pain VAS.

Results: In the ITT population, *Rubus idaeus* leaf extract 400mg and 200mg after 12 weeks of treatment reduced pain measured by the VAS respectively of -10.93 (1.95) mm and -8.51 (1.92) mm compared to baseline, while placebo group had a -3.84 (1.89) mm reduction. The mean pain decrease induced by *Rubus idaeus* leaf extract was over -7 mm which is clinically relevant, and reached clinically statistical difference compared to placebo with the highest dose (p=0.017; 95% CI, -13.11 to -1.07). Interestingly, subgroup analysis on the participants with a BMI>25, highlighted clinically relevant pain reduction for the 400 and 200mg doses compared to baseline of respectively -13.36 (2.26) mm and -11.25 (2.14) mm (placebo = -0.37