baseline. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened after the lso third year of follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups but were significantly higher in patients with erosive compared with non-erosive disease after the third year of follow up.
Conclusion: The findings of this study show that pain and number of painful and clinically swollen joints associated with US-detected synovial changes and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

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THU0454 CONDITIONED PAIN MODULATION AND TEMPORAL SUMMATION IN PERSONS WITH HAND OSTEOARTHRITIS AND ASSOCIATIONS WITH PAIN SEVERITY

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Background: Conditioned pain modulation (CPM) assesses adequacy of descending modulatory pathways. Temporal summation (TS) reflects ascending facilitation of nociceptive signals in the central nervous system (central sensitization). Inadequate CPM and enhanced TS of pain are both known to contribute to pain in chronic pain conditions. Different pain phenotypes may respond to different treatments strategies and may therefore be important to assess in clinical practice. CPM has not previously been explored in persons with hand OA and its relation to pain severity is unknown.
Objectives: To examine the prevalence of CPM and central sensitization alone or in combination in persons with hand OA, and to explore their associations with pain severity.
Methods: These cross-sectional analyses included 248 participants with hand OA from the Nor-Hand study. Participants reported hand pain severity during the last 24 hours on a numeric rating scale (NRS, 0-10). CPM was tested with pressure pain threshold (PPT) at the left wrist before (PPT1) and during (PPT2) a painful ischemic cuff conditioning stimulus at the opposite upper arm. Adequacy of CPM was calculated as CPM-ratio (PPT1/PPT2). CPM-ratio < 1 (increased PPT) indicates adequate CPM, while CPM-ratio $\geq$ 1 (unchanged/decreased PPT) indicate inadequate CPM. TS, increase in perceived pain to repetitive noxious stimuli as a marker of central sensitization, was assessed using mechanical punctate probes. We defined presence of TS as an increase in pain of $\geq$2 points on an NRS (0-10) during a repetition of ten punctate stimuli. We analyzed whether groups having adequate CPM and no TS, inadequate CPM only, TS only, or having both inadequate CPM and TS were associated with hand pain severity. We used linear regression analysis adjusted for age, sex, BMI, use of analgesics, education level, sleep disturbance, the Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and radiographic hand OA severity (Kellgren Lawrence sum score).
Results: Of the 248 participants included, 90% were women, median age was 61 (IQR 57, 66) years and mean BMI was 26.3 (SD 4.7) kg/m^2. CPM-ratio ranged from 0.4 to 1.6 (mean 0.9, SD 0.2), and 32% showed inadequate CPM. Presence of TS was found in 46% of the study population. Overall, 38% had no TS and adequate CPM, 29% had inadequate CPM only, 16% TS only and 16% had both (Table). We found that persons with inadequate CPM only and TS only reported higher pain severity than persons with adequate CPM and no TS (Table). Those with both inadequate CPM and TS reported similar levels of pain as persons with inadequate CPM only and TS only.

Abstract THU0454 – Table 1. Associations of conditioned pain modulation (CPM) and temporal summation (TS) with pain severity in persons with hand OA, (n=248)

	Mean (SD) NRS hand pain	Adjusted beta (95%CI)
No TS and adequate CPM (n=96)	3.2 (1.8)	0.0 (ref.)
Inadequate CPM-only (n=39)	3.9 (2.3)	1.1 (0.4, 1.8)
TS-only (n=73)	4.2 (2.5)	0.8 (0.3, 1.4)
TS and inadequate CPM (n=40)	4.6 (2.3)	1.1 (0.4, 1.8)

Adjusted for age, sex, BMI, analgesics, education, sleep disturbance, Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and Kellgren Lawrence sum score.
Conclusion: One third of persons with hand OA had inadequate CPM. Those with inadequate CPM, central sensitization or both reported higher pain severity than persons without any signs of altered central pain processing. Having both inadequate CPM and central sensitization was not associated with higher pain severity than having only one of the features. Our results are the first to demonstrate such a heterogenous variety of clinically relevant pain phenotypes in persons with hand OA.
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THU0455 PHARMACOKINETICS (PK) OF A SINGLE INTRA-ARTICULAR (IA) INJECTION OF CNTX-4975 (TRANS-CAPSAICIN) VS TOPICAL 8% CAPSAICIN PATCH

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Background: CNTX-4975 is in phase 3 trials for treatment of moderate to severe pain associated with knee osteoarthritis (OA). PK data from prior studies of CNTX-4975 in subjects with moderate to severe knee OA pain suggest low systemic and short-term exposure, similar to the FDA-approved topical capsaicin 8% patch.
Objectives: We compared single-dose systemic exposure to *trans-* and *cis*-capsaicin following IA injection of CNTX-4975 (>99.5% *trans*-capsaicin, <0.5% total impurities) with 8% capsaicin patch in subjects with moderate to severe knee OA pain.
Methods: This open-label, crossover study enrolled adults aged 50–75 y with moderate to severe knee OA pain in $\geq$1 knee (most painful knee, index knee; nonindex knee, no to mild pain [0–1; NPRS 0–4 scale]). Subjects were randomized 1:1 to 2 sequences: A (CNTX-4975 1 mg IA, index knee) followed by B (topical capsaicin 8% patch, posterior rib cage for 60 min) or BA sequence, with $\geq$7-day washout between treatments. Plasma samples for *trans-* and *cis*-capsaicin concentration assays were taken before and at specified times after study treatment. PK parameters, including maximum observed plasma concentration (C_{max}), area under the plasma concentration-time curve from time 0 to last quantifiable plasma concentration (AUC_{0-t}) and to infinity ($AUC_{0-\infty}$), time to C_{max} (T_{max}), and half-life ($t_{1/2}$), were determined. PK parameters were reported using descriptive statistics. Geometric means ratios of ln-transformed AUC_{0-t}, $AUC_{0-\infty}$, and C_{max} were evaluated using ANOVA.
Results: Sixteen subjects (median age, 62 y; female, 62.5%) were randomized to treatment (PK analysis population). T_{max} showed more rapid absorption of *trans*-capsaicin from IA CNTX-4975 vs the topical patch (**Table**). AUC_{0-t} and C_{max} indicated greater *trans*-capsaicin exposure

with CNTX-4975 vs the patch; however, exposure was short term, with mean $t_{1/2}$0.5 h. *Cis*-capsaicin concentrations were insufficient for calculating PK.

Conclusion: *Trans*-capsaicin from CNTX-4975 injection was rapidly absorbed and eliminated. The extent of systemic exposure to *trans*-capsaicin was significantly higher after CNTX-4975 vs the 8% capsaicin patch.

Abstract THU0455 –Table 1.

***Trans*-Capsaicin PK**

Parameter	IA CNTX-4975 1 mg N=14[a]	Topical 8% Capsaicin N=16[a]
AUC_{0-t}, h•pg/mL	n=14	n=15
Mean (SD)	3477.72 (1935.045)	257.57 (353.759)
GM (% CV)	3035.61 (55.6)	85.10 (137.3)
Geometric LS mean	2930.10	81.72
GM ratio[b] (90% CI)	35.85 (15.00–85.71)	
$AUC_{0-\infty}$, h•pg/mL	n=13	n=0
Mean (SD)	3668.85 (1888.667)	
GM (% CV)	3287.05 (51.5)	
Geometric LS mean	3113.42	
GM ratio[b] (90% CI)	NE	
C_{max}, pg/mL	n=14	n=16
Mean (SD)	3875.79 (2101.535)	123.28 (134.076)
GM (% CV)	3371.88 (54.2)	0 (108.8)
Geometric LS mean	3305.31	72.05[c]
GM ratio[b] (90% CI)	45.88 (23.87–88.18)	
T_{max},[d] h	n=14	n=16
Median (range)	0.2 (0–1)	1.0 (0–8)
$t_{1/2}$, h	n=13	n=0
Mean (SD)	0.54 (0.201)	

BLQ, below limit of quantification; CV, coefficient of variation; GM, geometric mean; LS, least squares; NE, not estimable.
[a]N=no. of subjects in PK population; [b]CNTX-4975/8% capsaicin patch; [c]n=15; 1 subject had C_{max}=0 and could not be included in log-transformed data analysis; [d]BLQ plasma concentrations before T_{max} were set to 0, except for BLQ value occurring between 2 measurable concentrations, which was set to missing. BLQ concentrations after T_{max} were set to missing.

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THU0456 EVALUATION OF THE USE OF ORLISTAT IN THE COMPLEX TREATMENT OF OBESITY IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Currently in the world there is a pandemic of obesity, which leads to an increase in diseases associated with overweight. Obesity is an important factor in the development and progression of osteoarthritis (OA). The metabolic phenotype of OA, which is directly associated with obesity, is highlighted. Due to the growing number of patients with obesity and OA, a high level of comorbidity and the lack of effectiveness of non-drug therapy, the problem of the effectiveness and safety of the therapy of obesity is very relevant.

Objectives: To evaluate the efficacy and safety of drug therapy for obesity in patients with OA of the knee.

Methods: 50 female patients (45-65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI>30kg/m²). Patients in Group 1 (n = 25) took 120 mg of orlistat 3 times a day in combination with a low-calorie diet and exercise for 6 months. Patients in Group 2 (n = 25) were on a low-calorie diet combined with exercise for 6 months. All patients initially received various non-steroidal anti-inflammatory drugs (NSAIDs) in tablet form. All patients were assessed for body mass, parameters of the WOMAC index, EQ-5D quality of life index, NSAID consumption, and orlistat therapy safety assessment.

Results: After 6 months of drug therapy for obesity, patients from Group 1 achieved a significant weight loss by 10.07% (p <0.05). Patients from Group 2 the use of non-medical methods of treating obesity reduced body weight by 0.84% (p> 0.05). Patients from Group 1 improved the WOMAC index: pain decreased by 52.5% (p <0.05), stiffness by 47.98% (p <0.05), and functional insufficiency by 51.55% (p <0.05). Patients from Group 2 also showed a decrease in the WOMAC index, but these changes were worse than in patients with greater weight loss. Patients from Group 1 showed a significant improvement in the quality of life for the EQ-5D index by 52.27% (p <0.05). Patients from Group 2 against the background of insignificant changes in body weight, the quality of life index EQ-5D did not change. The need to take NSAIDs on the background of drug therapy for obesity and weight loss decreased by 4.6 times. On the contrary, in Group 2 of patients on the background of non-pharmacological treatment of obesity after 3 months of observation, the need for NSAIDs was maintained in 76%. The need for NSAIDs in patients of Group 2 decreased 1.3 times. In general, the tolerability of orlistat in patients of Group 1 was good. Adverse reactions were observed in two patients in the form of steatorrhea. The appearance of an undesirable reaction was associated with errors in nutrition (eating food saturated with animal fats), which did not require discontinuation of the drug. After correcting the diet, no adverse reactions were noted in patients.

Conclusion: The results of our study showed a significant decrease in body weight by more than 10% in the group of patients with OA while receiving orlistat. Significant weight loss helps reduce pain intensity, improve joint function, improves the quality of life of patients with OA, reduces the need for NSAIDs, which can help stabilize other comorbid diseases in patients with OA and obesity. The study noted good safety of therapy with orlistat; no serious adverse reactions were reported. Thus, drug therapy for obesity using orlistat can be included in the management of patients with OA and obesity, who cannot achieve weight loss using non-drug methods.

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THU0457 EVALUATION OF THE EFFECTIVENESS OF COMPLEX TREATMENT OF OBESITY ON THE CLINICAL MANIFESTATIONS OF KNEE OSTEOARTHRITIS AND THE DYNAMICS OF CYTOKINES, DEPENDING ON THE DEGREE OF WEIGHT LOSS

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Background: Obesity is a risk factor and progression of the metabolic phenotype of osteoarthritis (OA). The decrease in body weight is important in the treatment of OA. Non-drug therapy aimed at altering the eating behavior, allows you to achieve a decrease in body weight of only 5%, which does not always contribute to the achievement of the clinical effect in patients with diseases of the joints.

Objectives: Assess the effectiveness of complex treatment of obesity with the use of orlistat (intestinal lipase inhibitor) on the clinical manifestations of the knee OA and the dynamics of cytokines (CRP, IL-6, TNF-α) depending on the degree of weight loss.

Methods: 50 female patients (45-65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI>30kg/m²). Patients in Group 1 (n = 25) took 120 mg of orlistat 3 times a day in combination with a low-calorie diet and exercise for 6 months. Patients in Group 2 (n = 25) were recommended non-drug therapy for obesity for 6 months. At baseline and after 6 months, the clinical parameters of the knee OA (WOMAC) were evaluated, the quality of life was assessed (EQ-5D). A laboratory study of peripheral blood was conducted at baseline and after 6 months: CRP, IL-6, TNF-α.

Results: After 6 months of complex treatment of obesity with the use of orlistat, patients in Group 1 achieved a significant weight loss of 10.07% (p <0.05). Depending on the degree of weight loss in Group 1, 15 patients lost> 10% and 10 patients lost 5–9.9% of the initial body weight. In the 2nd group, an insignificant weight loss of 0.84% (p> 0.05) was achieved, all patients in Group 2 lost less than 5%. Depending on the degree of weight loss, it is noted that in patients with weight loss more than 5% better than WOMAC (pain, stiffness, functional state) (p <0.05), EQ-5D (p <0.05) compared with less weight loss. In patients with weight loss> 10%, a significant decrease in CRP level was observed (p = 0.03) (Fig. 1) compared with baseline and patients with a 5–9.9% weight loss (p = 0.03) and <5% (p = 0.02). Data for statistically significant changes