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-∞} , 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-∞} , 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.
^aN=no. of subjects in PK population; ^bCNTX-4975/8% capsaicin patch; ^cn=15; 1 subject had C_{max}=0 and could not be included in log-transformed data analysis; ^dBLQ 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