Methods: The study involved 60 female patients with knee OA having neuropathic pain component (NPC; DN4 >4). Mean age 59.82±4.6 years (min 49, max 65 years). All patients were randomly divided into two groups to be treated with 2 therapeutic regimens: acetaminophen + pregabalin (Group I) or acetaminophen (Group II) for 5 weeks (3 visits). All patients were subjected to clinical and neurological examination, total WOMAC score assessment, verification of neuropathic pain (NP) (questionnaire DN4 and Pain DETECT), and VAS pain intensity assessment at rest.

Results: The therapy was successful in both groups with respect to WOMAC score [figure 1] (Group I – 1385.3±365.83 vs 1034.70±402.37 vs 886.64 ±456.31; Group II – 1206.04±358.72 vs 1016.45±428.52 vs 976.55 ±408.02 respectively, p=0.01). Significant reduction of pain intensity at rest was documented in both groups [figure 2]. Group I 61.60±14.91 vs 45.34±16.14 vs 36.24±18.09; Group II 56.07±22.58 vs 44.86±18.68 and vs 41.96±24.04, p=0.01, respectively. Therapeutic regimens in both groups had positive impact on NP based on DN4 questionnaire and Pain DETECT scores. However, a combination of a NSAID with anticonvulsants agent (pregabalin) resulted in a more pronounced effect. Changes in DN4 values in Group I (visit1/visit3) were: 5.97 ±1.24/2.97±1.83 p=0.001; and in Pain DETECT values – 17.93±3.87/9.34±6.18, p=0.001; while in Group II DN4 scores were 5.35±0.93/3.79±2.29, p=0.001; and Pain DETECT – 15.03±5.26/12.24±6.29 p=0.02. [figures 3–4].

Conclusions: Complex therapy with the use of Pregabalin in patients with OA of the knee, with signs of NPC, allows not only effectively reduce pain intensity and improve functional activity of patients and, consequently, the quality of life.

Disclosure of Interest: None declared


NEUROPHYSIOLOGICAL DATA IN PATIENTS WITH CHRONIC PAIN IN KNEE OSTEOARTHRITIS

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Background: Traditionally, chronic pain in OA is considered to be a classical model of nociceptive pain. Nociceptive mechanism can’t explain the presence: referred pain, secondary hyperalgesia and other sensitive phenomena. Recent studies has shown that besides nociceptive pain there is another mechanism that takes place in chronic pain OA – central sensitisation. Explores of chronic pain OA can be reached only by a complex approach in examining patients with chronic knee OA that includes not only a rheumatological examination, but examination of the neurological sphere and algometria. At the moment there are only few studies dedicated to neurophysiological changes in pain OA.

Objectives: to assess pain system with neurophysiological examination in chronic pain OA

Methods: 46 chronic knee pain OA and 23 healthy group control women, 45–65 years old, were included. The study included clinical rheumatologic, neurological examinations, neuropathic pain scales (DN4 and Pain DETECT). Knee X-ray and ultrasound studies. Neurophysiological examination included algometria with algometer and wind-up phenomena observed by Neuropen. Five test sites in the peripatellar region and one control site on tibialis anterior (5 cm distal to the tubial tuberosity) were located and marked for examination

Results: Neuropathic pain scales demonstrated neuropathic descriptors present in OA patients. Neurological examination revealed no somatosensory deficit. But examination of the sensitive sphere indicated hyperalgesia: primary hyperalgesia (increased sensitivity to pain in the damaged joint) and secondary hyperalgesia. OA can be reached only by a complex approach in examining patients with OA.

Conclusions: Complex therapy with the use of Pregabalin in patients with OA of the knee, with signs of NPC, allows not only effectively reduce pain intensity and improve functional activity of patients and, consequently, the quality of life.

Disclosure of Interest: None declared

STRUCTURAL EFFECTS OF INTRA-ARTICULAR SPRIFERMIN IN SYMPTOMATIC RADIOGRAPHIC KNEE OSTEOARTHRITIS: A POST-HOC ANALYSIS OF CARTILAGE AND NON-CARTILAGINOUS TISSUE ALTERATIONS OF THE 2-YEAR DATA FROM A 5-YEAR RANDOMISED, PLACEBO-CONTROLLED, PHASE II STUDY

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Background: Sprifermin, a recombinant human fibroblast growth factor 18, is currently being investigated as a potential disease-modifying osteoarthritis (OA) drug. Recently, a dose-dependent increase in femorotibial cartilage thickness, as well as medial and lateral compartment cartilage, over two years was reported1. Objectives: The aim of this post-hoc analysis is to evaluate potential effects of sprifermin on other joint tissues assessed, and no safety concerns raised. Methods: Patients aged 40–85 years with symptomatic radiographic knee OA, KLG 2 or 3, and medial mSwS ≥2.5 mm in the target knee were randomised (1:1:1:1:1) to receive double-blinded placebo or sprifermin (30 µg or 100 µg), administered as 3 weekly intra-articular injections in cycles every 6 or 12 months. 1.5T or 3T MRIs were acquired at baseline, 6, 12, 18 and 24 month follow-up visits using a standard protocol (ClinicalTrials.gov Identifier: NCT01033984). MRI analyses were performed using the Whole-Organ Magnetic Resonance Imaging Score (WORMS) system (time points of baseline, 12 and 24 months) by three trained musculoskeletal radiologists. Analyses of all sprifermin and placebo arms included multiple MRI-defined osteoarthritis features and multi-dimensional assessment: (a) delta-subregional approach (the difference in the number of subregions with worsening as compared to improvement) and (b) delta-sum approach (absolute scores of all subregions). Results: 549 patients were included. Dose-dependent treatment effect on cartilage morphology, in addition to the previously reported effect on cartilage thickness. Sprifermin was also associated with BML improvement in the patello-femoral joint. There were no significant effects associated with sprifermin on other joint tissues assessed, and no safety concerns raised.

REFERENCE:

A SAFETY, TOLERABILITY, PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) STUDY WITH INCREASING ORAL DOSES OF GLPG1972 ADMINISTERED DAILY FOR 29 DAYS SHOWS A STRONG Biomarker EFFECT IN PATIENTS WITH KNEE AND/OR HIP OA

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Background: Osteoarthritis (OA) is characterised by structural changes of the joint, of which degradation of articular cartilage is one of the major signs1. The main proteoglycan component of the extracellular matrix of articular cartilage is aggrecan. GLPG1972 as a potent and selective inhibitor of ADAMTS-5, a key aggrecan-cleaving enzyme involved in cartilage degradation, is being developed as a potential disease-modifying OA drug (DMOAD). Aggrecan cleavage by ADAMTS-5 results in release of N-terminal AGS neo-epitope fragments of which serum levels significantly decreased in healthy subjects treated with GLPG1972 during 14 days in a previous study2.

Objectives: To assess safety, tolerability, PK and PD (serum AGS-aggrecan levels) during and following administration of GLPG1972 in patients with knee and/or hip OA. Methods: This was a single centre, randomised, double-blind, placebo-controlled, age and gender stratified, ascending dose Phase Ib study, with three semi-sequential cohorts of 10 patients each, randomised to active drug or placebo in a 4:1 ratio. Doses tested were once daily 100, 200 and 300 mg. Treatment duration was 29 days. Patients had follow-up visits 14 and 21 days after last dose for additional PD assessments. Methods for PD have been described previously³. Results: Thirty patients were included. Of these, 24 patients were fully evaluable for safety and 22 were evaluable for PK (MF rate 8/16, 14 aged 50–64 and 10 aged 65–75) received active medication. All adverse events (AE) were mild and transient. No serious AEs were reported during the study; one female patient in the 300 mg group was discontinued after 15 days of treatment due to drug-related elevated transaminase values which returned to normal 9 days later while her bilirubin levels remained normal. There were no overall differences in lab abnormalities over time or significant changes in vital signs, ECG and Holter parameters. Steady state in plasma exposure was reached after 3 days of dosing. Exposure increased dose-proportionally. Mean serum AGS levels (SEM) decreased steadily over time in all patients receiving GLPG1972: –40% (2.9), –46% (4.5) and –53% (2.8) at day 15 compared to baseline in the 100, 200 and 300 mg group respectively. These levels remained stable until last dose on day 29, then consistently returned to pre-dose levels for all groups 14 and 21 days after last dose. Placebo group levels remained unchanged. Conclusions: When administered daily for 29 days in patients with knee and/or hip OA, GLPG1972 at oral doses of 100, 200 and 300 mg q.d. was generally well tolerated and safe. Serum AGS levels, as a marker for target engagement and potential proxy of cartilage degradation, showed a dose-dependent decrease over time up to 53% below baseline in the 300 mg group. These PK-PD findings are consistent with what we observed in a previous study in healthy subjects4 and reinforce the rationale for developing GLPG1972 as a DMOAD.

REFERENCES: