were no statistically significant group differences for any of the secondary patient-reported outcomes at week 68.

Conclusions: A significant weight reduction improves the knee OA patients' symptoms, as a high proportion of patients experience an OMERACT-OARSI response at 16 weeks. However, although the sustainability of weight loss was significantly better in the diet group, this trial did not provide any evidence of a difference between continuous attention from a dietician following a 1-year maintenance program compared to either exercise or 'nothing' in terms of treating OA symptoms.

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A MULTICENTRE, INTERNATIONAL, DOUBLE BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF 2 DIFFERENT REGIMENS OF HYADD4-G IN KNEE OSTEOARTHRITIS

K. Pavelka1, F.J. Niethard2, N. Giordani3
1Inst. of Rheumatology, Prague 2, Czech Republic; 2Univ.klinikum und Poliklinik der RWTH, Aachen, Germany; 3Fidia Farmaceutici SpA, Padova, Italy

Purpose: Hyaluronic acid (HA) has been included in European League Against Rheumatology, Osteoarthritis Research Society International, American College of Rheumatology, American Pain Society and American Academy of Orthopedic Surgeons recommendations for treatment of painful knee osteoarthritis (OA). Intra-articular (IA) sodium hyaluronate has proven efficacious and well tolerated for the treatment of pain associated with knee OA, but optimal molecular weight of HA and dosing regimen is still not known. HYADD4-G is a novel hydrogel obtained with a high viscoelastic properties than the native HA with preservation of hyaluronic biocompatibility.

The study objective was to evaluate the efficacy and tolerability of 2 different HYADD4-G dosing regimens (2 versus 3 i.a. injections) against phosphate-buffered saline (PB-Saline) up to 6 months in patients with knee OA.

Methods: Prospective, multicentre, parallel, randomized, double-blind (masked observed), PB-Saline controlled, 6 months study in knee OA. Patients: primary knee OA according to ACR criteria, Kellgren-Lawrence II-III stage, pain on walking >40 mm on VAS at baseline. Primary outcome measure: pain during 50 ft (15 m) walk test, measured by Visual Analogue Scale (VAS) at visits 2-9. Statistical Analysis: efficacy evaluated in intent-to-treat (ITT) population. Two-sided superiority tests of 2 different regimens of HYADD4-G vs PB-saline for all primary and secondary outcome measures.

Results: A total of 439 patients were randomized either to HYADD4-G 2 inj. group (n=145), HYADD4-G 3 inj. (n=150) and PB-saline (n=144). There were no significant differences in demographic and disease activity parameters between groups at baseline. Symptomatic outcome measures showed a significant improvement from baseline in the three treatment groups. In particular, considering the HYADD4-G 2 injections group, the mean change (%) between baseline and final visit for the 50 ft walk test (VAS) was -36.5 mm (-58.9%), for WOMAC pain -19.8 mm (-40.4%), for WOMAC Stiffness -20.5 mm (-27.1%), and for WOMAC physical function -18.2 mm (-35.4%). However, due to a huge and unexpected placebo response, for primary and secondary endpoints, no statistically significant differences between the treatment groups at any of the Visits 5 to 9 were observed. In exploratory sub-group analysis of patients with age <65 years the pain in the target knee was improved from baseline Visit 2 to Visit 5 in all treatment groups. The comparison regarding pain in the target knee during walk test between the HYADD4-G 2 injections group and the PB-Saline group for patients <65 years revealed the following p-values: P=0.1561 at the first visit after the last injection (day 28), P=0.0267 at day 60, P=0.0397 at day 90, P=0.0499 at day 120, and P=0.3329 at day 180 [2-sided t-test].

There were no clinically relevant and/or statistically significant differences between the treatment groups with regard to frequency, distribution, intensity, premature termination, or seriousness, but for probable relationship to study group and occurrence of AEs in target knee.

Conclusions: New HA formulations HYADD4-G were effective and well tolerated in symptomatic treatment of painful knee OA. The reductions in VAS knee pain for patients <65 years were significantly more effective in HYADD4-G given in a 2 IA injections than PB-saline. A clinically significant decrease in analgesic consumption, was also observed in the same HYADD4-G study group.

Keywords: osteoarthritis, hyaluronic acid, IA therapy.

Reference

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EFFICACY AND SAFETY OF 2 PROPRIETARY BASED CHONDROITIN SULPHATE MEDICINAL PRODUCTS: STRUCTUM® 1000MG (500 MG BID) AND CHONDROSULF® 1200MG (400 MG TID) IN 837 PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS (KOA)

P. Fardellone1, M. Zaim1, E. Mahieu2, A.-S. Saurel2
1Rhumatology Dept., CHU Amiens, Amiens, France; 2Inst. de Recherche Pierre FABRE, Ramonville Saint-Agne, France; 3Rhumatology Dept., St Antoine Hospital, Paris, France

Purpose: To compare the efficacy and safety of 2 proprietary based Chondroitin Sulphate medicinal products: Structum® 1000mg and Chondrosulf® 1200mg.

Methods: Multicentre, randomized, double-blind, double placebo, active controlled, parallel-group study, conducted according to a non-inferiority design. Patients aged 50-80 years with symptomatic KOA (ACR criteria) were randomized to receive during 24 weeks either Structum 500mg BID or Chondrosulf 400mg TID. Inclusion criteria were: global pain in the target knee ≥ 40 mm on a 100-mm visual analog scale (VAS), Lequesne’s Algofunctional Index (LFI) score > 7 (range: 0-24) and radiological Kellgren-Lawrence grade 2 or 3. The primary outcome was the mean variation over 24 weeks of the global pain (VAS) and LFI score. Main secondary outcomes were patient’s and physician’s global assessments, Omeract-OARSI responder rates, concomitant analgesics intake and quality of life (SF-12). Safety was assessed by recording any adverse events (AE). A non-inferiority test was performed: 95% confidence interval (CI) of the difference between groups on change of VAS and LFI scores. Predefined non inferiority limit was settled as the lower limit of the 95% CI above -5mm and -1pt respectively for VAS and LFI scores.

Results: 837 patients were randomized: 817 analyzed in the full analysis dataset (FAS), 692 in the per protocol (PP) analysis with no difference between groups at entry regarding demographics and disease characteristics. The main efficacy analysis (PP) showed no difference between the 2 groups on the mean variations of pain VAS or LFI scores over 24 weeks which varied for VAS and LFI scores by -23.9 (17.5) and -3.2 (2.4) respectively in Structum group and by -23.8 (17.2) and -3.1 (2.4) in Chondrosulf group. Differences for VAS and LFI were respectively 0.01 [IC95%: -2.6; 2.6] and 0.139 [IC95%: -0.2; 0.5]. The lower limit of the 2 CI were above the predefined non inferiority margins (-5 and -1 respectively), clearly demonstrating the non inferiority of Structum compared to Chondrosulf. The analysis on the FAS gave similar results. Analyses of the secondary efficacy outcomes (PP and FAS) populations showed the same trends for each treatment with improvements of clinical relevance at W24. The overall improvement

Figure 1

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