MCID values. Effect estimates of pharmacologic knee OA treatments were also extracted from recent high-quality meta-analyses, and the effect of IA-saline or topical placebo was used as an adjustment for meta-analyses that used IA-saline or topical placebo as a comparator, respectively. This was done to estimate the therapeutic effect of these treatment options when compared to a truly null treatment option, as IA-saline has been shown to not be a null-effect intervention. The unadjusted and adjusted treatment effect values were compared across an MCID value range of 0.2 to 0.5 standard deviation units representing an effect size range. This range was used to determine if the adjustment for the effect of IA-saline would affect the potential clinical interpretation of the previously published meta-analysis results.

Results: IA-saline provides a therapeutic benefit that is potentially clinically meaningful to patients based on a range of MCID values (figure 1). Across the same range of MCID values, the effects of high molecular weight IA-hyaluronic acid products and IA-corticosteroid treatments were not conclusively clinically significant. However, when reassessing these treatments while accounting for the treatment effect of IA saline, they were found to have a clinically significant effect at the strictest MCID value (figure 2).

Figure 1. Effects of Topical Placebo and IA-Saline in Comparison to the MCID Threshold Range

Figure 2. Pain Effect Estimates Adjusted for Placebo Effect Estimate (from Bannuru et al [2015])

Conclusions: The use of IA-saline as a placebo treatment within RCTs of IA injectable therapies is inappropriately underestimating the true effect of these treatments. When the potential therapeutic effect that IA-saline demonstrates is accounted for, these IA therapies show a considerably larger therapeutic effect.

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SAT0566 ASSOCIATIONS OF OSTEOCLASTS AND MACROPHAGES IN SUBCHONDRAL BONE WITH SYMPTOMS IN PEOPLE WITH KNEE OA

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Background: Knee pain is a major source of disability and reason for hospital visits in patients with knee OA, but the pain pathophysiology is incompletely

understood. Recent accumulating clinical evidence indicates that subchondral bone plays a role in generating joint pain in OA¹. Subchondral bone marrow lesions (BMLs) detected on magnetic resonance imaging (MRI) in knee OA are strongly associated with pain¹. In human OA histology, bone turnover and osteoclast numbers in subchondral bone were increased². Inflammatory CD68-positive macrophages have been detected in bone marrow compartments of subchondral bone tissue from tibial plateaux of OA knees³. However, the relevance of osteoclasts and macrophage infiltration in subchondral bone to knee OA symptoms has not been clarified.

Objectives: To identify osteoclast and macrophage infiltration in subchondral bone associated with symptomatic knee OA, by comparing cases with similar macroscopic chondropathy, half of whom had sought help for knee pain and undergone total knee replacement (TKR) surgery (symptomatic chondropathy), the other half of whom had not sought help for knee pain but had died from unrelated illness (asymptomatic chondropathy).

Methods: Medial tibial plateaux were obtained from people undergoing TKR for OA (symptomatic chondropathy), and from post-mortem (PM) cases matched for similar macroscopic chondropathy scores (asymptomatic chondropathy). Samples were histologically graded for chondropathy, subchondral fibrovascular or macrophage infiltration, and TRAP-positive osteoclasts were quantified (figure 1).

Results: Patient demographics are shown in table 1. Total Mankin score showed similar values between the two groups (Table 2). The number of osteoclasts in symptomatic chondropathy cases was significantly higher than in asymptomatic chondropathy cases (table 2). This difference remained significant (p<0.05) after adjusting for age by logistic regression analysis. However, there was no significant difference in macrophage densities between symptomatic and asymptomatic chondropathy groups (Table 2).

Abstract SAT0566 – Figure 1. Representative photomicrographs of TRAP-positive osteoclasts and CD68-positive macrophages in subchondral bone.

Abstract SAT0566 – Table 1. Patient demographic data.

	PM Asymptomatic chondropathy	TKR Symptomatic chondropathy	p
Number	31	31	
Male/Female	19/12	16/15	0.442
Years (mean ± SD, median (IQR))	75 ± 11 74 (68, 84)	65 ± 10* 67 (56, 73)	0.001
Revised SFA score (mean ± SD, median (IQR))	69 ± 17 74 (68, 84)	69 ± 17 76 (57, 79)	0.955
Grade IV chondropathy score (mean ± SD, median (IQR))	30 ± 27 30 (0, 48)	30 ± 27 30 (0, 48)	0.943

SFA; Systeme Franc, aise D'Arthroscopie * : p<0.05 by Mann-Whitney U test

SFA; Sytème Franc, aise D'Arthroscopie
*: p<0.05 by Mann-Whitney U test

Abstract SAT0566 – Table 2. Histopathological characteristics.

	PM Asymptomatic chondropathy	TKR Symptomatic chondropathy	p
Total Mankin score (mean ± SD, median (IQR))	8.8 ± 2.7 8 (7, 11)	9.1 ± 2.4 9 (7, 11)	0.755
Fibrovascular tissue(n)	14	11	0.437
Osteoclasts (number / cm)	1.1 ± 3.2 0 (0, 0.8)	3.3 ± 5.7* 1.0 (0, 2.7)	0.019
CD68+ macrophages grading(0-2) (mean ± SD, median (IQR))	1.13 ± 0.76 1 (1, 2)	1.06 ± 0.51 1 (1, 1)	0.626

* : p<0.05 by Mann-Whitney U test

*: p<0.05 by Mann-Whitney U test

Conclusions: Our results showed that not macrophages but osteoclast infiltration in subchondral bone were associated with symptomatic knee OA. Osteoclasts release protons that generate a local acidosis, which might be a potent activator of nociceptors leading to increased pain signaling⁴. Increased osteoclast activity might be key features associated with bone pain in knee OA.

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SAT0567

THE LEADING RISK FACTORS FOR DEVELOPING INTENSIVE PAIN SYNDROME IN THE KNEE JOINTS IN PATIENTS WITH OSTEOARTHRITIS

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Background: Intensive pain is one of key predictors of OA progression, although it remains unclear which key factors are responsible for the development of intensive pain.

Objectives: To study the risk factors for developing intensive knee pain in OA pts in a multicenter prospective study.

Methods: A prospective 5 year study included 185 female-patients from 6 RF territorial entities aged 40–75 y. with confirmed knee OA (ACR criteria), stages I–III (Kellgren J.-Lawrence J.), who signed an informed consent. Mean age was 59 ± 8,1 y., the age at knee pain onset was 49 ± 8,7 y., and average OA duration was 11 ± 8,4 y. Individual annual medical file included patient's anthropometric parameters, case history, clinical examination findings, evaluation of knee pain intensity by VAS, WOMAC scale, the knee joint status, comorbidities and therapeutic modalities used during the follow up period. Instrumental diagnostic methods included plain radiography of knee joints, dual energy X-ray absorptiometry (DEXA) of the lumbar spine, femoral neck and of subchondral bone of the hip and tibia, ultrasonography (US) and MRI examination of knee joints. Stage II of knee OA was documented in 135 (73%) out of 185 pts, and stage III – in 50 (27%). Statistica 10.0 and SPSS 15.0 packages were used for statistical analysis.

Results: Based on pain intensity pts were divided into two groups: Group I – pts with more intensive pain (>70 mm VAS) – 16,8%, and Group II – pts with less intensive knee pain (<70 mm VAS) – 83,2%. Both groups were comparable in terms of age 58,8 ± 7,68 vs 61,06 ± 5,91 y., and disease duration 10^(5–17) vs 12^(6–18) y. Although, pts from Group I had statistically significantly higher body weight 82,7 ± 13,8 vs 74,8 ± 12 kg ($p=0,002$), higher pain estimations by WOMAC 374^(348–382) vs 225^(172–268) mm ($p<0,0001$), stiffness 100^(80–125) vs 80^(60–110) mm ($p=0,01$), FI 1102 (970–1238) vs 820(646–935) mm ($p<0,0001$) and total WOMAC 1541 (1462–1702) vs 1130(880–1291) mm ($p<0,0001$). Besides, pts from Group I had greater percentages of varus knee deformity – 80,6% vs 29,2% (RR=2,76, 95% CI 2,04–3,73, $p<0,0001$) and of H.valgus 87,1% vs 59,1% (RR=1,47, 95% CI 1,22–1,78, $p=0,002$). MRI showed higher rate of bone marrow oedema in medial tibia in Group I: 51,9% vs 31,1% (RR=1,67, 95% CI 1,07–2,59, $p=0,03$) compared to pts from Group II with less pronounced pain. A multivariate (discriminant) analysis showed that the most important risk factors for developing intensive knee pain in OA pts were: significant functional impairment, presence of knee varus deformity and Heberden's nodes, cartilage abnormalities (MRI finding) in medial tibial compartment, familial OA. A model capable of predicting development of intensive knee pain in an individual patient with high accuracy (area under the ROC-curve 0.910 (95% CI 0,860–0,961) has been developed based on identified RF and their coefficients. Model accuracy is 87%.

Conclusions: In a prospective multicenter study, using comprehensive instrumental modalities (knee radiography, ultrasonography, MRI and BMD of peripheral bones and subchondral hip and tibia) it has been demonstrated that intensive knee pain (>70 mm VAS) is caused by excessive functional impairment, presence of knee varus deformity, Heberden's nodes, OA in parents, and cartilage destruction in the medial tibial compartment.

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SAT0568

EFFECT OF DIACERIN VS GLUCOSAMINE-CHONDROITIN ON DISEASE PROGRESSION, AND MEASURES OF FUNCTION IN PERSONS WITH KNEE OSTEOARTHRITIS: A 2-YEAR RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Background: Globally, the incidence of knee osteoarthritis (KOA) is increasing. The treatments available for many years have included both pharmacological and non-pharmacological modalities.

Objectives: To examine whether Diacerein is more effective than glucosamine-chondroitin or a placebo in slowing disease progression, physical functioning and/or pain in patients with mild-moderate knee osteoarthritis

Methods: In a double-blind RCT, 322 Pakistani patients between 40–65 years with mild to medium KOA (Kellgren-Lawrence Grading 2 or 3) and a history of knee pain >6 months were randomised to receive Diacerein (50 mg twice daily) or Glucosamine-chondroitin (1200 mg twice daily) or a placebo (twice daily) for 2 years. All groups received exercise, diet and pain management counselling. Participant's general health and knee condition was assessed at baseline, 6-, 12-, 18- and 24 months using Short Form³⁵ Health Survey (SF 36) and WOMAC Index respectively. The Cartilage Oligomeric Matrix Protein (COMP) test was carried out at baseline, 12- and 24 months to assess progression of Knee OA. Improvement was considered at least a 10 point increase in SF36 score from baseline; a 10 point decrease in WOMAC and a 1 unit decrease in COMP.

Results: Participants with complete data at the end of year 1 (n=226) and year 2 (n=191) were analysed. At baseline, no significant differences were found in the distribution of gender, age, BMI, COMP levels, SF36, WOMAC scores as well as KL grade levels. Compared to baseline, at year 1 and 2 follow-up, participants in the Diacerein group had statistically significant improvement in their ability to work and other physical activities in comparison with those in the other 2 groups. By the end of year 2, social functioning improved in the Diacerein group as compared to those in the Glucosamine-Chondroitin (GC) group. Compared to placebo group, social functioning improved in the Diacerein group. A greater proportion of GC and placebo group participants reported reduction in their fatigue levels than those in the Diacerein group (p value=0.007). Using the SF36 scale, in comparison to baseline, improvements were made in all the groups albeit with no between group differences for physical functioning, emotional well-being, and general health. Using the WOMAC index, improvement occurred in all its domains of pain, stiffness and physical functioning, but statistically larger proportion of stiffness reduction took place in the GC group.