factors including sonographic features of synovial inflammation or radiographic severity influence outcome. These results raise potential questions about the routine use of US to enhance or predict response to IACI in knee OA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2015-eular.6229

## THU0440 CLINICAL BENEFIT AND CARTILAGINOUS TISSUE REPAIR AFTER KNEE JOINT DISTRATION: 5 YEARS FOLLOW-UP

N.O. Kuchuk[1], K. Wiegant[1], J.-T. van der Woude[2], P.M. van Roermund[3,4], F. Eckstein[5], S.C. Mastbergen[1], F.P. Lafeber[1]. *[1]Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht; [2]Department of Orthopedics, Maartensclinic Woerden, Woerden; [3]Department of Orthopedics, University Medical Center Utrecht, Utrecht; [4]Department of Orthopedics, Medical Centre Amstelveen, Amstelveen, Netherlands; [5]Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University Salzburg, Salzburg, Austria*

**Background:** Placement of a total knee arthroplasty (TKA) in case of end-stage knee osteoarthritis (OA) in young patients is less successful than in elderly, with high revisions rates later in life (1). Recently knee joint distraction (KJD) showed results of clinical improvement and tissue structure modification in patients with knee OA (2) postponing a TKA. The duration of these beneficial effects is yet unclear.
**Objectives:** We evaluated whether the clinical improvement and tissue structure modification in knee OA sustain and persist on MRI and X-rays 5 years after distraction.
**Methods:** Patients (n=20; <60yrs) with tibio-femoral OA who were resistant to conservative therapy and eligible for TKA, were treated with 8 weeks of KJD by use of an external fixator. Clinical evaluation was performed by WOMAC, VAS pain and survival of the knee joint. Changes in cartilage thickness were quantified by MRI, and change in joint space width (JSW) was evaluated on standardized semi-flexed X-rays. The five-year changes after KJD were evaluated and were compared with the natural progression rate of OA in OsteoArthritis-Initiative participants with similar baseline characteristics.
**Results:** From 20 patients (age 49±6 yrs), two withdrew informed consent and three other patients were treated with TKP (after three and four years), so the survival of the knee joint was 80% at 5 years. Moreover, there was persistent clinical improvement compared to baseline sustaining over time: Δ WOMAC +21,1 points (CI:8,9-33,3; p=0.002), Δ VAS pain -27,6mm (CI:-13,3-42,0; p<0.001).
In addition, minimum radiographic JSW was increased at five years as compared to pre-treatment values: Δ+0,43mm (CI:0,02-0,84; p=0.040). Taking natural loss of cartilage thickness into account, this change was significantly different from the changes as a result of extrapolated natural progression (Δ-0,39mm and Δ-0,18mm, respectively) resulting at 5 years in a difference of +0,65mm (CI:0,07-1,23; p=0.031) and of +0,41mm (CI:0,07-0,74; p=0.020) for mean JSW on X-ray and average cartilage thickness on MRI, respectively.
**Conclusions:** In young OA patients, TKA can be postponed for at least five years in 80% of the patients. KJD treatment results in persistent clinical benefit and an increase in cartilage thickness and JSW.
The effects were not as strong as observed 1 and 2 years after treatment, still they represented a significant structural benefit compared to the natural course of the disease. Joint distraction has great potential to effectively postpone TKA and as such represents a promising therapeutic option for young patients with severe knee OA.
**References:**
[1] Julin J, Jamsen E, Puolakka T,et al. Younger age increases the risk of early prosthesis failure following primary total knee replacement for osteoarthritis. A follow-up study of 32,019 total knee replacements in the Finnish Arthroplasty Register. Acta orthopaedica. 2010;81(4):413-9.
[2] Wiegant K, van Roermund PM, et al. Sustained clinical and structural benefit after joint distraction in the treatment of severe knee osteoarthritis. Osteoarthritis and cartilage/OARS, Osteoarthritis Research Society. 2013 Nov;21(11):1660-7. PubMed PMID: 23954704.
**Acknowledgements:** This study was supported by the Dutch Arthritis Foundation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2015-eular.1604

## THU0441 RISK-BENEFIT OF CO-ADMINISTERED TRAUMEEL® (TR14) AND ZEEL® (ZE14) INTRA-ARTICULAR (IA) INJECTIONS IN PATIENTS WITH MODERATE-TO-SEVERE PAIN ASSOCIATED WITH OA OF THE KNEE (OAK)

C. Lozada[1], E. del Rio[2], D.P. Reitberg[2], R. Smith[2], R.W. Moskowitz[3]. *[1]University of Miami Miller School of Medicine, Miami, FL; [2]Rio Pharmaceutical Services, LLC, Bridgewater, NJ; [3]University Hospitals Case Medical Center, Cleveland, OH, United States*

**Background:** Data for Tr14&Ze14, a combination of dilute biological and mineral components was recently reported to be effective in treatment of OAK.[3] In a recent meta-analysis of OAK pain from 129 studies/32129 patients (Pt)[1], IA placebos (Pb) were significantly superior to oral Pb. Statistically normalized (Hedges g)[2] effect sizes (ES) at 3 months compared to IA-Pb were: IA-hyaluronates (HA) 0.34, IA-corticosteroids (C) 0.32, diclofenac 0.23, ibuprofen 0.15, naproxen 0.09, celecoxib 0.04, acetaminophen (indeterminable).
**Objectives:** To qualitatively assess risk-benefit; guide clinical utility of Tr14&Ze14 relative to other treatments (Tx).
**Methods:** Patients (Pt) with OAK randomized to 3 weekly IA injections of either Tr14&Ze14 or saline.[3] Primary efficacy variable was change in knee pain from Baseline to End-of-Study (Week 17) measured by WOMAC OA Pain Subscale (Section A, 1-5) 100 mm VAS (WOP). ES were calculated for comparison to meta-analysis data.[2] Safety was assessed by monitoring vital signs, target-knee physical examinations, adverse events, concomitant medications, and regulatory databases (PSURs/DSURs).
**Results:** 232 Pt (All Tr14&Ze14, n=119, All Pb, n=113; Intention-to-Treat Tr14&Ze14, n=117, Pb, n=111). As expected, Tr14&Ze14 did not discriminate for WOP after only 1 of 3 injections on Day 8 (p=0.371), but subsequently was significantly superior to Pb (p<0.05) on Days 15, 43, 57, 71, 85 and 99 (primary endpoint); approached significance on Day 29 (p=0.0686, Figure 1). ES compared to IA-Pb were 0.26, 0.22, 0.30, 0.31, 0.30, 0.25 and 0.25 for Days 15, 29, 43, 57, 71, 85 and 99, respectively, indicating persistent efficacy over time with values comparable or superior to independently reported IA and oral Tx. Also, for 50'walk pain, Tr14&Ze14 was significantly superior to Pb (p<0.05) on all Days post-Day 8 except Day 29 (p=0.0501). There were no related SAEs; other AEs were generally mild and mostly unrelated to treatment. PSURs/DSURs confirmed a favorable safety profile; Tr14 exposure was at least 117,333,284 ampoules or 2,257,043 Pt-years with cumulative 7 serious and 39 non-serious possibly-related ADRs; Ze14 was at least 30,168,795 ampoules or 580,169 Pt-years with a cumulative 0 serious and 9 non-serious ADRs.

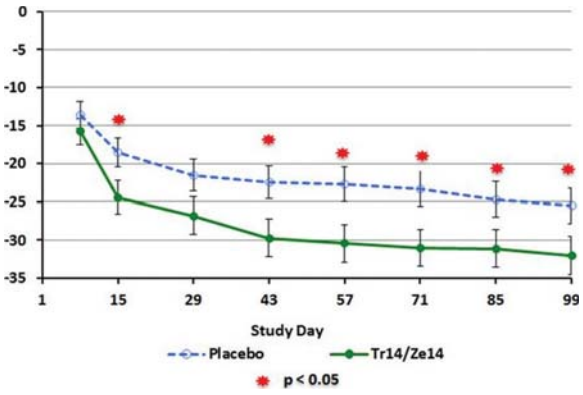


Figure 1. Mean (±SE) WOMAC A Changes from Baseline (ITT Population, N=228).

**Conclusions:** Tr14&Ze14 provided statistically significant and clinically relevant pain relief on days 15 to 99 in comparison to Pb in a double-blind, randomized, controlled trial.[3] Efficacy ES were consistent with those observed for IA-HA, IA-C and oral NSAIDs. Unlike oral NSAIDs, the safety profile was benign with no signals of cardiovascular, gastrointestinal or other concerning risks. From a qualitative perspective, the risk-benefit relationship for Tr14&Ze14 appears favorable, particularly compared to oral NSAIDs.
**References:**
[1] Bannuru et al. Ann Intern Med; 162: 1/6/15:p46-54.
[2] Cooper & Hedges. The Handbook of Research Synthesis. New York: Russell Safe Foundation; 1994.
[3] Lozada, C., del Rio, E., Reitberg, DP., Smith, R., Kahn, C., and Moskowitz, RW. Arth Rheumat 66 (10) Suppl.: S1266 (Abstr 2896).
**Disclosure of Interest:** C. Lozada Consultant for: Rio Pharmaceutical Services, LLC; HEEL USA, E. del Rio Consultant for: Biologische Heilmittel Heel GmbH, D. Reitberg Consultant for: Rio Pharmaceutical Services, LLC, R. Smith Consultant for: Rio Pharmaceutical Services, LLC, R. Moskowitz Consultant for: Rio Pharmaceutical Services, LLC; HEEL USA
**DOI:** 10.1136/annrheumdis-2015-eular.4268

## THU0442 KNEE JOINT DISTRACTION COMPARED WITH TOTAL KNEE PROSTHESIS: A RANDOMIZED CONTROLLED TRIAL (PRELIMINARY RESULTS)

J.-T. van der Woude[1], K. Wiegant[1], R.J. van Heerwaarden[2], S. Spruijt[3], P.M. van Roermund[4], S.C. Mastbergen[1], F.P. Lafeber[1]. *[1]Rheumatology & Clinical Immunology, UMC Utrecht, Utrecht; [2]Orthopedics; [3]Maartenskliniek, Woerden; [4]Orthopedics, Medical Centre Amstelveen, Amstelveen, Netherlands*

**Background:** Placement of a total knee prosthesis (TKP) in case of end-stage knee OA in young patients is less successful than in the elderly, with high revision rates of up to 44% later in life. [1,2] However, in severe end-stage knee OA, effective joint saving treatments are scarce. Recently, knee joint distraction (KJD) showed results of clinical improvement and cartilaginous tissue repair in patients with knee OA. [3] However, no comparative data on efficacy is available. A RCT was set out and determined whether there was a clinical relevant difference between KJD and TKP in clinical outcome 1-year after treatment.