FRI0017 INFLIXIMAB (ANTI-TNF ALPHA ANTIBODY) TREATMENT FOR RHEUMATOID ARTHRITIS: INTERIM ANALYSIS OF A SPANISH COHORT STUDY PERFORMED IN ROUTINE PRACTICE. A MULTICENTER OPEN-LABEL STUDY OF THE CATALAN SOCIETY OF RHEMATOLOGY, CATALUNYA, SPAIN

J Carbonell. *Rheumatology, Hospital Del Mar, Barcelona; Hospital Mutua Terrassa; Hospital Vall d'Hebrón, Barcelona; Hospital Clínic, Barcelona; Hospital Parc Taulí, Sabadell; Clínica Girona; Hospital de Vic, Barcelona; Hospital de Malalties Reumàtiques, Barcelona; Hospital Sant Rafael, Barcelona, Spain*

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Background

Objectives To evaluate the efficacy and safety of infliximab for RA in daily clinical practice.

Methods We included 54 patients with refractory RA who failed at least two different DMARDs (including MTX). The patients received 3 mg/kg infliximab at weeks 0, 2, 6 and the every 8 weeks for 54 weeks. MTX and all other concomitant medications were kept at a stable during the study. Evaluations before each infusion included tender (TJC) and swollen joint counts (SJC), patient and physician global assessments, pain score (VAS), HAQ, morning stiffness, and ESR. All adverse events were recorded. We used the Wilcoxon test for two related samples to assess differences between measures taken in pairs.

Results All patients received at least 2 infusions and 9 patients completed the study through week 22, when this analysis was done. ACR components including TJC, SJC, morning stiffness, patient and physician global assessments, VAS pain, ESR and the HAQ significantly decreased at week 2 (with $p < 0,001$ for all these ACR components), as it is shown in Table 1. At week 6, all these ACR components showed values significantly decreased ($p < 0,001$) with relation to week 0 but not in comparison with week 2 (except for TJC, SJC and physician global assessment with $p < 0,01$). The results for clinical response and HAQ did not reach statistical significance after week 6, due to the small number of patients that completed treatment in week 14 ($n = 24$) and in week 22 ($n = 9$). One patient dropped out because of major surgery (related to the RA). The treatment was well tolerated; only minor adverse events ($n = 15$) without any serious infection were noted.

Abstract FRI0017 Table 1

	Week 0 n = 54	Week 2 n = 54	Week 6 n = 44	Week 14 n = 24	Week 22 n = 9
TJC	17,0	14,0	8,0	4,5	8,0
SJC	12,0	7,0	5,0	5,0	7,0
Morning stiffness	60,0	15,0	7,5	10,0	15,0
ESR	48,0	30,0	35,0	32,0	33,0
Patient Global Assesment	68,5	48,0	49,5	32,0	36,0
Physician Global Assesment	66,5	50,0	46,5	46,0	49,0
HAQ	2,00	1,62	1,62	1,44	1,75

Median Values.

Conclusion Patients with refractory rheumatoid arthritis significantly improve during therapy with infliximab. The observed beneficial effect is maintained during the treatment period without major adverse events.

FRI0018 PROTECTION BY PHOSPHODIESTERASE-4 INHIBITOR ROFLUMILAST OF MICE AGAINST COLLAGEN-INDUCED ARTHRITIS

¹J Barsig, ²B Leung, ¹DS Bundschuh, ¹L Wollin, ¹R Beume, ²FY Liew. ¹Department of Pharmacology, Byk Gulden, Konstanz, Germany; ²Department of Immunology, University of Glasgow, Glasgow, UK

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Background Orally available small molecular weight compounds with ability to suppress the proinflammatory mediator Tumour Necrosis Factor alpha (TNF) are of high interest for the treatment of rheumatoid arthritis (RA). Roflumilast (3-cyclopropyl-methoxy-4-difluoromethoxy-N-[3,5-di-chloropyrid-4-yl]-benzamide) is a highly potent and selective inhibitor of phosphodiesterase type 4 (PDE4), that effectively suppresses TNF production *in vitro* and *in vivo*.^{1,2} This compound is currently in clinical development for asthma and COPD.

Objectives We investigated the capacity of Roflumilast to reduce the release of TNF *in vivo* in mice, and also examined its antiarthritic potential in murine collagen-induced arthritis (CIA).

Methods For induction of systemic TNF release, male BALB/c mice were injected intraperitoneally with lipopolysaccharide (LPS, *S. abortus equi*, 5 mg/kg). Mice were orally treated with 1 or 10 mg/kg of Roflumilast 30 min prior to LPS challenge. Plasma was obtained 90 min after challenge for determination of cytokines by ELISA. CIA was induced in male DBA/1 mice by intradermal injection of 200 µg of type II collagen (CII) in Freund's complete adjuvant, followed by a booster injection of CII on day 21 (200 µg in PBS i.p.). Roflumilast (1 or 5 mg/kg) was given once daily p.o. on days 23-33. Arthritic scores (0-3) and paw thicknesses were monitored between days 21-39. In parallel experiments, groups of mice were sacrificed and cells from draining lymph nodes were restimulated *in vitro* with graded concentrations of CII. TNF, Interleukin-6 (IL-6), and Interferon-gamma (IFN), released within 72 h of *in vitro* culture, were measured by ELISA. Histological analysis was performed on joints taken on day 35 after primary immunisation.

Results Roflumilast dose-dependently suppressed LPS-induced TNF production *in vivo* (75% with 10 mg/kg). By contrast, plasma levels of the anti-inflammatory cytokine Interleukin-10 were substantially raised (500% with 10 mg/kg). In addition, Roflumilast dose-dependently protected mice against CIA. This was also evident histologically by a significant reduction of joint inflammation and bone/cartilage erosion. The *in vitro* capacity of lymph node cells to produce TNF, IL-6, and IFN upon CII-stimulation was markedly reduced, even when cells were prepared one week after withdrawal of drug treatment.

Conclusion These data demonstrate that Roflumilast is a promising candidate for the oral treatment of rheumatoid arthritis.

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FRI0019 EFFICACY OF ETANERCEPT ON TENOSYNOVITIS AND RHEUMATOID NODULES

MJ Kaiser, MC Bozonnat, C Jorgensen, JP Daures, J Sany. *Immuno-Rheumatology, Lapeyronie Hospital, Montpellier, France*

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Background Etanercept is an efficient treatment of Rheumatoid arthritis (RA), but the effect on extraarticular features remains unknown.

Objectives To evaluate the efficacy of etanercept on extraarticular features of RA.

Methods We looked for tenosynovitis, rheumatoid nodules in 87 patients (70 women, 17 men) with RA or juvenile rheumatoid arthritis (JRA), at day 0, before beginning treatment with Etanercept (25 mg twice a week) and at day 180 of treatment. The population included 82 cases of RA and 5 cases of JRA, rheumatoid factor positive in 64 cases, median age 51 years (7–76). The median duration of RA was 11 years (2–32) and the median number of previous treatments was 5 (1–10).

Results The evolution of the median value of modified DAS 28 was highly significant, with a score of 4.0 at day 0 and 1.7 at day 180 ($p = 0.01$). At day 180, 72 patients could be assessed for the 3 parameters studied. At day 0, 72 patients out of 87 had tenosynovitis. All tenosynovitis disappeared in 12 patients, some but not all tenosynovitis disappeared in 7 patients. New tenosynovitis appeared at day 180 in 8 patients, 45 patients remained unchanged.

Moreover, 22 nodules were counted in 10 patients out of 87 assessed at day 0. At day 180, the assessment remained unchanged. Nodules neither appeared nor disappeared. No other extraarticular features appeared during treatment.

Conclusion Etanercept is an effective inhibitor of TNF α providing clinical and biological improvement in both RA and JRA. However, Etanercept had no efficacy on tenosynovitis and rheumatoid nodules.

FRI0020 RADIAL HEAD EXCISION IMPROVED FLEXION CONTRACTURE IN ELBOW SYNOVECTOMY WITH RHEUMATOID ARTHRITIS

T Oshige, H Tsurukami, A Sakai, N Okimoto, T Nakamura. *Department of Orthopaedic Surgery, University of Occupational and Environmental Health, Japan, Kitakyusyu, Japan*

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Background Swett¹ was the first to report a successful elbow synovectomy in chronic infection arthritis. Smith-Petersen *et al.*² added radial head excision for rheumatoid arthritis elbow synovectomy. However, the usefulness of radial head excision in elbow synovectomy was controversial.

Objectives This study was designed to clarify the usefulness of radial head excision in elbow synovectomy with rheumatoid arthritis.

Methods We performed elbow synovectomy for 19 patients (21 elbows) suffering from rheumatoid arthritis. There were 14 women and 5 men. Radial head excision (E group) was added in 7 patients (7 elbows) and radial heads retain (R group) was in 12 patients (14 elbows). Average age at the time of the surgery was 51.4 years in E group, and 52.8 years in R group. The follow up period averaged 6.4 years in E group and 9.1 years in R group.

We evaluated clinical results and radiological parameters preoperatively and final examination. Clinical results were evaluated include pain, range of motion, stability.

Pain score was classified 4 stages. (0: no pain, 3: severe pain). We defined instability as more than 20 degrees of varus-valgus motion with the elbow flexed 25 degrees. Radiographic parameters were measured the height of humerus (H) in anteroposterior radiograph, the thickness of olecranon (O) in lateral. The degree

of joint destruction was elucidated by Larsen grade. We compared with preoperative and final examination in each group. Statistical analysis was performed by Wilcoxon signed-ranks test. A p value of less than 0.05 was considered to indicate a significant difference.

Results Pain was eliminated or improved in all patients at final examination. The average pain score changed 2.7 to 0.7 in E group and 2.5 to 0.3 in R group. The flexion contracture preoperatively was -42.5 degrees, and significantly improved to -26 degrees at final examination in E group. In R group, it was not significantly improved from -35.7 degrees to -30.1 degrees. The arc of flexion did not change after synovectomy both two groups (115 to 124 in E group, 122 to 115 in R group). One elbow in each group was considered to be unstable at final examination.

Larsen grade had deteriorated 1 grade or more in all elbows of each group. The value of H significantly decreased 8.4 mm to 3.9 mm in E group and 11.0 mm to 6.2 mm in R group. The value of O was significantly decreased 12.8 mm to 10.0 mm in E group and 13.7 mm to 11.7 mm in R group.

Conclusion Radial head excision improved flexion contracture without influences on pain, stability and radiographic change in elbow synovectomy with rheumatoid arthritis.

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FRI0021 COMBINATION THERAPY WITH CYCLOSPORIN-A AND METHOTREXATE IN PATIENTS WITH EARLY POTENTIALLY AGGRESSIVE RHEUMATOID ARTHRITIS, A RANDOMISED DOUBLE BLIND PLACEBO CONTROLLED TRIAL

¹AH Gerards, ²RB Landewé, ¹AP Prins, ³GA Buijn, ²HS Goei Thè, ¹BA Dijkman. ¹Rheumatology, Vrije Universiteit Medical Centre, Amsterdam; ²Rheumatology, University Hospital Maastricht, Maastricht; ³Rheumatology, Medical Centre Leeuwarden, Leeuwarden, The Netherlands

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Background Patients with advanced RA with a suboptimal response on low dose methotrexate (MTX) have shown to respond well after the addition of cyclosporin-A (CsA).¹ The combination of CsA and MTX has never been tested in a parallel design in patients with early RA.

Objectives To assess in patients with early, and potentially aggressive RA whether combination therapy with CsA and MTX compared to CsA mono therapy, results in a higher number of clinical improvements.

Methods 120 RA-patients with active disease who were rheumatoid factor positive (95%) and/or had signs of radiological damage (49%) received CsA and MTX or CsA and placebo for 48 weeks. MTX was started at a dose of 7.5 mg/week, and increased to 15 mg/wk at week 16. CsA was started at a dose of 2.5 mg/kg/day and increased to a maximum of 5 mg/kg/day. Patients who did not have an ACR20 response after 24 weeks were withdrawn. ACR responses at the 20%, 50% and 70% levels were calculated on basis of intention to treat with the last visit put forward in case of premature discontinuation.