

Table 1. In-group comparison before and after the study

	Before		p
	Median (IQR 25/75)	After Median (IQR 25/75)	
Exercise Group (n=21)			
Peak Power (W)	354.73 (267.59/471.55)	441.3 (295.2/636.9)	<b>0.002*</b>
Peak Power (W/kg)	6.74 (5.44/8.94)	7.7 (6.4/9.7)	<b>0.001*</b>
Average Power (W)	291.5 (188.78/359.61)	360.0 (220.4/446.4)	<b>0.001*</b>
Average Power (W/kg)	5.54 (4.07/6.88)	6.0 (4.8/7.4)	<b>0.002*</b>
Control Group (n=21)			
Peak Power (W)	355.57 (225.43/463.62)	366.7 (236.3/447.8)	0.259
Peak Power (W/kg)	6.69 (5.80/7.83)	7.3 (6.1/8.1)	0.232
Average Power (W)	261.04 (181.68/351.27)	284.8 (187.8/373.0)	0.050
Average Power (W/kg)	5.29 (4.75/5.85)	5.5 (5.0/6.1)	0.076

Wilcoxon Test. IQR: Interquartile Range; W: watt; W/kg: watt/kilogram; \*p<0.05.

Table 2. The differences in the groups after 8 weeks

	Exercise Group (n=21)	Control Group (n=21)	p
	Median (IQR 25/75)	Median (IQR 25/75)	
ΔPeak Power (W)	65.1 (23.8/107.1)	24.5 (-15.6/39.4)	<b>0.009*</b>
ΔPeak Power (W/kg)	0.9 (0.3/1.6)	0.3 (-0.3/0.6)	<b>0.007*</b>
ΔAverage Power (W)	41.4 (9.9/78.7)	17.3 (5/31.3)	<b>0.019*</b>
ΔAverage Power (W/kg)	0.6 (0.3/1.3)	0.2 (-0.1/0.5)	<b>0.024*</b>

Mann-Whitney U Test. IQR: Interquartile Range; Δ: Delta; W: watt; W/kg: watt/kilogram; \*p<0.05.

**Conclusions:** The present study is the first study focusing on improving anaerobic capacity in children with JIA. According to our results, an 8-week water exercise program which is performed at the weekends might be beneficial to improve anaerobic exercise capacity in children with JIA.

**Disclosure of Interest:** None declared

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WEDNESDAY, 14 JUNE 2017

## Assessment and management of osteoporosis

### OP0010 EFFECT OF DENOSUMAB COMPARED WITH RISEDRONATE IN GLUCOCORTICOID-TREATED INDIVIDUALS: RESULTS FROM THE 12-MONTH PRIMARY ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDY

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**Background:** Glucocorticoid (GC)-induced osteoporosis (GIOP) remains the most common secondary cause of osteoporosis. Despite approved therapies, many subjects do not receive GIOP prevention or treatment. There is increased RANKL and decreased osteoprotegerin (OPG) expression in patients with GIOP. Denosumab (DMAb) is a monoclonal antibody to RANKL. This study was designed to assess the safety and efficacy of DMAb compared with risedronate (RIS) in GC-treated individuals, in whom treatment guidelines advocate a GIOP intervention.

**Objectives:** The primary objective was to demonstrate, in separate GC-continuing (GC-C) and GC-initiating (GC-I) subpopulations, that DMAb was not inferior to RIS with respect to percentage change from baseline (%Δ) in lumbar spine (LS) bone mineral density (BMD) at 12 months. Secondary objectives were to assess superiority of DMAb over RIS with respect to %Δ in LS and total hip (TH) BMD at 12 months.

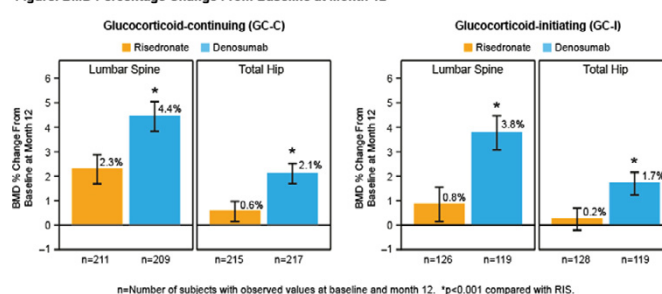
**Methods:** This was a phase 3, randomized, double-blind, double-dummy, active-controlled study to evaluate DMAb vs. RIS in GC-treated individuals for 24 months. Eligible subjects were women and men ≥18 yrs receiving GC therapy at a dose ≥7.5 mg prednisone daily or its equivalent for ≥3 months or <3 months prior to screening (GC-C and GC-I, respectively). All subjects <50 yrs were required to have a history of osteoporotic fracture. GC-C subjects ≥50 yrs were required to have a LS, TH, or femoral neck BMD T-score ≤-2.0; or a T-score ≤-1.0 with a history of osteoporotic fracture. Subjects were randomized 1:1 to SC DMAb 60 mg every 6 months or oral RIS 5 mg daily for 24 months. Subjects were to receive daily calcium (≥1000 mg) and vitamin D (≥800 IU) supplementation. Primary outcome was %Δ in LS BMD at 12 months (non-inferiority in GC-C and GC-I). Secondary outcomes included %Δ in LS and TH BMD at 12 months (superiority). The study remains blinded and is ongoing.

**Results:** A total of 795 subjects (505 GC-C and 290 GC-I) enrolled in the study. Baseline characteristics were balanced between treatment groups (Table). Non-inferiority and superiority with DMAb were demonstrated for both the GC-C and GC-I subpopulations, as indicated by significantly greater BMD gains compared with RIS at the LS and TH in both subpopulations (Figure). The incidences of adverse events (AEs) and serious AEs, including serious AEs of infection, as well as fracture, were similar between treatment groups and consistent with the known safety profile of DMAb.

Table. Baseline Characteristics

	Glucocorticoid-continuing (GC-C)		Glucocorticoid-initiating (GC-I)	
	Risedronate N=252	Denosumab N=253	Risedronate N=145	Denosumab N=145
Sex - n (%)				
Male	67 (26.6)	68 (26.9)	52 (35.9)	52 (35.9)
Female	185 (73.4)	185 (73.1)	93 (64.1)	93 (64.1)
Age (years) - mean (SD)	61.3 (11.1)	61.5 (11.6)	64.4 (10.0)	67.5 (10.1)
Medical conditions of interest - n (%)				
Rheumatoid arthritis	118 (46.8)	96 (37.9)	43 (29.7)	48 (33.1)
Polymyalgia rheumatica	18 (7.1)	20 (7.9)	52 (35.9)	50 (34.5)
Systemic lupus erythematosus	16 (6.3)	15 (5.9)	4 (2.8)	2 (1.4)
Daily prednisone-equivalent dose (mg) - mean (SD)	11.13 (7.69)	12.29 (8.09)	15.61 (10.25)	16.57 (13.01)
25 (OH) vitamin D (ng/mL) - median (Q1, Q3)	28.0 (23.6, 36.3)	29.2 (24.2, 37.6)	28.6 (24.2, 36.4)	28.8 (23.6, 36.0)
BMD T-score - mean (SD)				
Lumbar spine	-1.96 (1.38)	-1.92 (1.39)	-1.06 (1.57)	-0.92 (1.86)
Total hip	-1.56 (0.96)	-1.66 (0.96)	-0.98 (1.07)	-1.14 (1.00)

Figure. BMD Percentage Change From Baseline at Month 12



n=Number of subjects with observed values at baseline and month 12. \*p<0.001 compared with RIS.

**Conclusions:** DMAb significantly increased BMD more than RIS at the spine and hip at 12 months. The overall safety profile was similar between treatment groups. DMAb has the potential to become another treatment option for patients newly initiating or continuing GC who are at risk for fracture.

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## Systematic literature review: the link from science to clinical practice

### OP0011 DOES A VERY EARLY THERAPEUTIC INTERVENTION IN VERY EARLY ARTHRITIS / PRE-RHEUMATOID ARTHRITIS PATIENTS PREVENT THE ONSET OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND METANALYSIS

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**Background:** Recent progress in the understanding of rheumatoid arthritis (RA) pathogenesis leads to growing interest in the concept of pre-RA, a clinical stage in which very early intervention could be more efficacious.

**Objectives:** To assess the efficacy of very early therapeutic interventions in pre-RA patients, i.e., with either undifferentiated arthritis, or ACPA-positive arthralgia/arthritis (ie, very early RA, VERA), through a systematic literature review (SLR) and meta-analysis (MA).

**Methods:** The SLR was performed following Cochrane guidelines. The search used "undifferentiated arthritis" or "very early rheumatoid arthritis" (VERA) associated with "therapy" or "treatment", and was limited to randomized controlled trials (RCTs) published in English over the last five years. It was conducted in Pubmed, Embase and Cochrane RCT databases, as well as EULAR and ACR congress abstracts of the last two years. Two independent readers (SH, BH) extracted the following data through a standardized form: study quality, patient status at baseline (either undifferentiated arthritis or VERA), the type of intervention, and disease characteristics over time as well as occurrence of RA.

The main outcomes that were analysed for the meta-analysis were RA occurrence at 52 weeks and beyond and the absence of radiographic progression at week 52. The meta-analysis was performed using RevMan with Mantel-Haenszel method.

**Results:** The search identified 595 abstracts, of which 9 RCTs were finally selected (including 2 congress abstracts). Eight were related to undifferentiated arthritis; 1 to VERA. The studies included 1156 patients, weighted mean age 45.8+/-15.2 years, mean symptoms duration 16.2+/-12.6 weeks; 66.0+/-17.7% were female.

The occurrence of RA at week 52 or more was available in 7 studies (assessing 800 patients). Early therapeutic intervention – either methylprednisolone (80 to 120mg IM), methotrexate, TNF-blocker, abatacept or rituximab -reduced the risk of occurrence of RA with a pooled odds ratio (OR) of 0.72 (95% CI [0.54; 0.96]), p 0.02 (Figure).

There was no statistically significant difference between the treatments or placebo, for the absence of radiographic progression (pooled OR 1.36 [0.82;2.27])

The outcome was assessed at Week 52 for all studies, except for Van Dongen 2007 (PROMPT), where it was assessed at Week 120. MethylPDN, methylprednisolone; MTX, methotrexate.

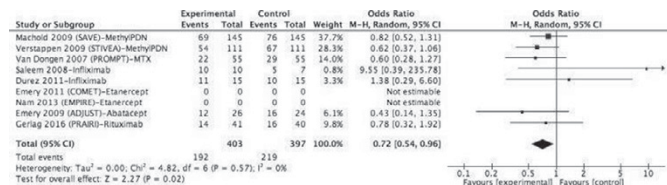


Figure 1. RA appearance at week 52 or more.

**Conclusions:** This meta-analysis demonstrates that early therapeutic intervention significantly reduces the risk of RA onset in pre-RA patients. The benefit /risk balance and feasibility in clinical practice remain to be further assessed.

**Disclosure of Interest:** None declared

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## EULAR Campaign: Don't Delay, Connect Today

### OP0012-PARE RHEUMATOSPHERE: REACH NEW HEIGHTS IN DIAGNOSIS AND TREATMENT OF ARTHRITIS BY ENGAGING, EMPOWERING AND INSPIRING

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**Background:** We aim to reach new heights in diagnosis and treatment of arthritis through research and we believe that part of this encompasses public engagement. Engaging the public is an essential part of scientific life, as the majority of work carried out by researchers is publically funded. Therefore the public are entitled to and should be encouraged to see the conclusions of this work in an easily accessible manner.

**Objectives:** 1) *Engage* the public about rheumatic disease, what it is, what it does to the body and how we, as scientists and clinicians, address unmet needs in this field.

2) *Empower* patients in order to help them understand their disease and treatments thereby improving patient satisfaction and compliance to therapy.

3) *Inspire* the next generation of scientist by encouraging children to study science at school and raise the profile of these subjects with education authorities and the government.

**Methods:** Rheumatosphere was established to address public engagement needs in the arthritis research field. We have used a variety of techniques to capture the attention of small and large audiences of all ages. Techniques include: Ultrasound scanning, coffee with a scientist at our cell cafe, posters displays, multidisciplinary classroom lessons in a school environment and comic book drawing. These resources and activities have been deployed at 5 major science events across Scotland in the last 3 years, and at the British society for rheumatology's annual conference in 2016. Further to this we have also attended regular events at the Glasgow science centre and schools across Scotland.

**Results:** During our first three major events we have had approximately 3000 encounters with the median age of participants being 33 years. Over half (51%) of the people that we engage with directly knew someone affected by rheumatoid arthritis. Engaging the public and patients with visualisation of their own joints using ultrasound is effective in demonstrating how joints function. This then serves as a starting point to highlight current research and celebrate the newer treatment strategies which have resulted in better outcomes for our patients. Feedback from our events show that people are keen to engage and learn more about arthritis, with 80% wanting to know more about autoimmunity and 83% wanting to know more about the clinical work going on throughout Glasgow.

Children at these events and in the classroom are encouraged to learn about the immune system and it's role in health and disease through the medium of comic books and art. Allowing the children to relate scientific topics to an

already established and popular media has proven to be an effective learning tool. In 2016, 94% of school pupils who interacted with Rheumatosphere said that they had learned something new about arthritis, including careers options through which they could become involved in helping to better understand and treat disease.

Our future plans include partnering with Government and National Science Centre stakeholders to further develop educational curricula in the arena of musculoskeletal science and immunology.

**Conclusions:** We feel that engaging with the public and patients is an essential part of our vocation as scientists and clinicians and only by empowering them will we be able to reach new heights in diagnosis and treatment of arthritis.

**Disclosure of Interest:** None declared

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WEDNESDAY, 14 JUNE 2017

## Standing Committee session on paediatric rheumatology

### OP0013 PULMONARY MANIFESTATIONS IN JUVENILE ONSET MIXED CONNECTIVE TISSUE DISEASE AFTER LONG-TERM DISEASE DURATION – A NORWEGIAN CASE-CONTROL STUDY

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**Background:** Pulmonary manifestations in mixed connective tissue disease (MCTD) are common and a major cause of morbidity and mortality [1]. Data on lung involvement in patients with juvenile onset MCTD (JMCTD) are scarce.

**Objectives:** The aim of this study was 1) to compare pulmonary function abnormalities in a nationwide representative Norwegian JMCTD cohort with that of matched controls, 2) investigate occurrence of interstitial lung disease (ILD) in JMCTD and 3) to evaluate possible associations between pulmonary findings and disease related variables.

**Methods:** Inclusion criteria were fulfillment of the Kasukawa or Alarcon-Segovia criteria and symptom-onset before 18 years. The control group was randomly drawn from the national population register, after matching for age and gender. Fifty-two patients with JMCTD were examined after mean disease duration 16.2 years, 44 (85%) were female. Patients and controls performed pulmonary function tests (PFT) and a 6 min walk test (6MWT). The patients had a high-resolution CT (HRCT) of the lungs.

**Results:** Abnormal PFT were found in 24 patients (46%) and in 12 controls (23%) (p<0.01) (table 1).

Variable	JMCTD patients	Controls	P value
Age at examination, years	28.0 (10.3)	29.0 (10.1)	0.61
BMI, kg/m <sup>2</sup>	22.7 (3.5)	23.4 (3.0)	0.29
Current smokers daily/occasionally, n (%)	7 (14)	9 (17)	0.59
Never smokers, n (%)	35 (67)	34 (65)	0.83
6MWD, meters	634.3 (76.5)	698.9 (86.6)	<0.01
FVC, litre	3.4 (0.6)	4.3 (1.0)	<0.01
FVC (% of predicted)	89 (14)	109 (11)	<0.01
FEV1, litre	2.9 (0.5)	3.5 (0.8)	<0.01
FEV1 (% of predicted)	89 (13)	102 (11)	<0.01
FEV1/FVC	0.86 (0.06)	0.82 (0.07)	<0.01
DLCO/VA (mmol/kPa min/l)	1.6 (0.2)	1.8 (1.0)	0.26
DLCO/VA (% of predicted)	88 (12)	92 (13)	0.14

More patients than controls had abnormal FVC (11 patients and 0 controls, p<0.01) and FEV1 (12 patients and 2 controls, p<0.01). Diffusing capacity for carbon monoxide adjusted for alveolar volume was abnormal in 12 patients and 8 controls (p=0.34). One patient and 3 controls had a pathological FEV1/FVC (less than 70% of predicted, p 0.62). HRCT showed ILD in 15 patients (29%). The extent of lung parenchyma involved was median 2% (range 1–75) in the patients with ILD. Two patients had more than 20% of lung parenchyma involved (graph 1). The most common abnormalities were reticular patterns, being present in 13 patients (25%). 2 patients (4%) had ground glass attenuation. We could not find correlations between the extent of ILD and PFT or 6MWT. There were no significant differences in PFT values or other disease related variables between the patients with and without ILD.

**Conclusions:** Patients with JMCTD had significantly reduced pulmonary function after mean 16.2 years disease duration compared to matched controls. However, overall lung function was only moderately reduced. The occurrence of ILD assessed with HRCT was 29%, but the majority of patients with ILD had mild disease. To our knowledge, this is the first systematic case-control study of pulmonary manifestations in JMCTD.

**References:**

[1] Gunnarsson R, Aalokken TM, Molberg O, et al. Prevalence and severity of interstitial lung disease in mixed connective tissue disease: a nationwide, cross-sectional study. *Ann Rheum Dis* 2012;71:1966–72.

**Disclosure of Interest:** None declared