(IBD) with a variable clinical course. Common findings include enthesitis and dactylitis. Current treatments include anti-TNFa and anti-IL-12/IL-23 antibodies with varying success rates but the involvement of several pro-inflammatory cytokines suggests that other targeted therapies may be effective. Notably, the JAKs (a family of 4 non-receptor tyrosine kinases) are crucial for the signaling of many pro-inflammatory cytokines. In this regard, the JAK1-selective inhibitor filgotinib (GLPG0634, GS-6034) demonstrated clinical efficacy in patients with rheumatoid arthritis, a disease that shares some hallmarks with PsA and Crohn's disease, making this molecule a potential therapeutic tool for the treatment of PsA.

Objectives: Filgotinib was evaluated at the dose of 30 mg/kg/d (*per os*) in a mouse model of PsA induced by overexpression of IL-23.

Methods: Overexpression of IL-23 was induced by hydrodynamic delivery of mIL-23 enhanced Episomal Expression Vector (SBI) to male B10.RIII mice[1]. Evolution of inflammation of the paws and fingers was assessed by clinical scoring as well as *in vivo* molecular imaging (Bruker In-Vivo Xtreme imaging system). Enthesis and fingers were collected for expression analysis of inflammatory genes and target-related biomarkers. Neutrophil infiltrate, as well as pSTAT3 positive cells, were analyzed using immunohistochemistry in Achilles' enthesis and subcutaneous area, respectively. Colon was collected for lesion score determination as well as inflammatory and target-related biomarker gene expression.

Results: High levels of IL-23 were maintained during the time-course of the study and were correlated with severity of finger and paw swelling. Localization of the fluorescent signal using ProSense™ imaging was asscociated with inflammation of enthesis and finger reported in PsA. Moderate inflammation of the colon was also observed. Filgotinib significantly improved clinical scoring and tended to prevent neutrophil/granulocyte infiltrate in paw (with significant effect being showed at earlier time point). Filgotinib reversed some up-regulated inflammatory genes in enthesis and/or fingers (CCL20, CXCL1, IL-22, MMP9 and TNFa) and reduced the target-related gene Mx2. Filgotinib significantly counteracted pSTAT3 induction in the subcutaneous area further demonstrating target engagement in the diseased tissue. Finally in line with previous findings[2], Mx2 expression in colon was slightly reversed by filgotinib.

Conclusions: In a mouse model of PsA, filgotinib improved global clinical score and decreased signs of inflammation in hindlimbs. Target engagement both in hindlimbs and colon was also demonstrated. These data support the evaluation of filgotinib in patients with PsA.

References:

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THURSDAY, 15 JUNE 2017

Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design

OP0162-PARE | **AN EXPLORATION OF LIVED EXPERIENCES AMONGST ADULTS WITH RHEUMATOID ARTHRITIS USING AN ONLINE RESEARCH COMMUNITY PLATFORM: A PILOT STUDY**

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Background: Online technology has revolutionised the way in which people connect and share their experiences. It also brings new opportunities to engage patients in health and social care research through the use of an online research community platform (ORCP). For example, it can improve the accuracy and usefulness of information gathered about research priorities, and it can be used to understand behaviours and preferences. Given an increasing prevalence of long-term conditions including rheumatoid arthritis, online technology represents a novel route for participation and engagement in research.

Objectives: To explore the benefits and limitations of an ORCP through understanding lived experiences of adults with rheumatoid arthritis.

Methods: We used a purposive sampling approach to ensure variation of key attributes amongst people with rheumatoid arthritis. A total of eight individuals used the ORCP during the pilot study. Qualitative data were collected through online focus groups, conducted as semi-structured interviews and asynchronous

threaded discussions. The study was conducted in line with fieldwork guidelines, and written informed consent was obtained.

Results: The closed ORCP enabled a physically disconnected group to share their experiences of living with rheumatoid arthritis, describing the symptoms, diagnostic experience and support they received. In addition, participants shared their experiences and opinions about treatment delivery and adherence, the impact of rheumatoid arthritis, and the experiences of transitional care from paediatric to adult health services, where appropriate. Reasons and feeling about research participants and drug development processes were also discussed.

Conclusions: Our pilot study provided important accounts from people living with rheumatoid arthritis, highlighting the substantial impact of the disease on their daily lives. The ORCP removed physical contact between the researcher and participants, the absence of which may enable a richer data collection. However, it also has its limitations, primarily because the researcher is less able to gauge participants' attitudes and concerns. ORCPs represent a novel route of data collection, enabling researchers to immerse themselves into a community of individuals, whether they are patients, carers or professionals.

OP0163-PARE | **INVIGORATING THE PRINCIPLE OF PARTICIPATORY RESEARCH IN GERMANY - SETUP OF A TRAINING COURSE FOR PATIENT REPRESENTATIVES**

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Background: Patient participation in research projects is important because it enhances the legitimacy of research projects and facilitates the implementation of research results after completion of the respective projects. Since 2009, patient representatives have been actively involved in EULAR projects, and the first EULAR training course for patient representatives was conducted in 2010.

Objectives: The aim of the project was to create a training course for German-speaking patient representatives and thereby to invigorate the principle of participatory research in Germany. The training course is supposed to enable patients to make valuable contributions in research projects. In addition the training course aimed at lowering barriers and strengthening the patients' self-confidence, in order to facilitate their integration in the unfamiliar environment among researchers.

Methods: Participants were trained during a two-day interactive training course. For evaluation of the course, each participant anonymously answered 14 questions in a questionnaire.

Results: The training course consists of seven modules. In the first module (I), the history of the EULAR "patient research partners" is described and the tasks of the future German patient research partners are outlined. In the following modules, various types of research and study designs (II), the generation of research questions and hypotheses (III), various scientific tools (IV), the detailed sequence of steps in a typical research project (V), literature research in scientific databases (VI) and the process of reviewing grant applications (VII) are explained. Each module is subdivided in an explanatory section, an exercise section (where the participants have to apply the newly achieved skills) and a final discussion section.

So far, two courses have been conducted. The training course was rated either "very good" or "good" by 77% and 23% of the participants, respectively. Those patients, already actively involved in research projects, acclaim participatory research as interesting and enriching.

Conclusions: The training course was perceived very well by the participants. In future follow-up meetings, the usefulness of the various modules and any missing items will be discussed and the training course adapted accordingly.

THURSDAY, 15 JUNE 2017

Osteoarthritis: new horizons for treatment

OP0164 | **OPTIMIZING RECRUITMENT CRITERIA FOR AN OSTEOARTHRITIS STRUCTURE MODIFICATION TRIAL: DATA FROM THE OAI**

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Background: The design of clinical trials for osteoarthritis is challenging; structural changes in tissues are quantitatively small and proceed very slowly. No clear guidance exists on how to optimise recruitment. KL grade is a poor recruitment criterion as centres interpret KL differently. Quantitative measures should be

better, and metric radiographic joint space width (rJSW) is related to subsequent risk of radiographic progression. Although new MRI measures provide increased responsiveness in DMOAD trials, it is unknown whether selecting for recruitment based on radiographic criteria are well suited for responsiveness of these new measures.

Objectives: (1) To determine which baseline rJSW values are associated with most subsequent progression for rJSW, MRI cartilage and bone outcomes (2) Explore baseline covariates that influence progression rates (3) Estimate the trial numbers needed using the criteria determined by steps (1) and (2).

Methods: We used all knees from the Osteoarthritis Initiative which had all 3 measures recorded (rJSW – Duryea method; MRI cartilage thickness & bone area, Imorphics) at baseline, 1 and 2 years. We categorised knees into bins of 1mm rJSW, and assessed the 2 year changes of each bin, and characterised the distribution of rJSW in KL 0 knees. We used ANCOVA models to consider which covariates (including gender, height, weight, alignment, age, pain severity) affected 2-year slope of change, and responsiveness using SRM. For the final optimised recruitment groups, we calculated SRMs (CIs assessed using the bootstrap method of Efron) and derived the number of patients per arm in a putative trial.

Results: 4796 knees were included (2789 females, mean age 61.45). The lower 95th percentile values for rJSW in women and men were 3.9 and 4.5mm respectively. The mean changes at 2-years for all 3 outcomes were greatest for the categories of 2–3 and 3–4mm baseline rJSW (Figure 1A) with notably little change in knees with rJSW<2mm. Of the covariates, only pain improved responsiveness. Using a total WOMAC pain criterion; ≥3/20 reduced numbers from 726 knees to 331 knees, and improved 1 year SRM (95% CI) from 0.27 (0.17,0.34) to 0.41 (0.29,0.51) in rJSW, from 0.45 (0.37,0.51) to 0.55 (0.45,0.65) in MRI cartilage and from 0.60 (0.52,0.66) to 0.73 (0.62,0.83) in MRI bone. Figure 1B shows the relative SRMs for the 3 outcomes based on 2 inclusion criteria (rJSW 2–4mm and pain ≥3/20; n=331) and demonstrates the required trial numbers (with confidence intervals) based on the SRMs.
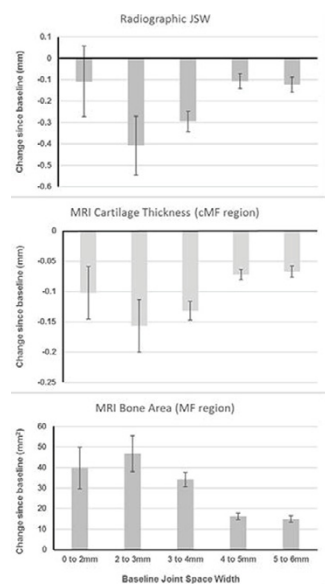

Figure 1A: Mean 2-year change for 3 imaging outcomes by baseline rJSW

Units are in mm for rJSW and MRI cartilage thickness, and in mm² for MRI bone area (95% confidence limits for change since baseline in brackets)
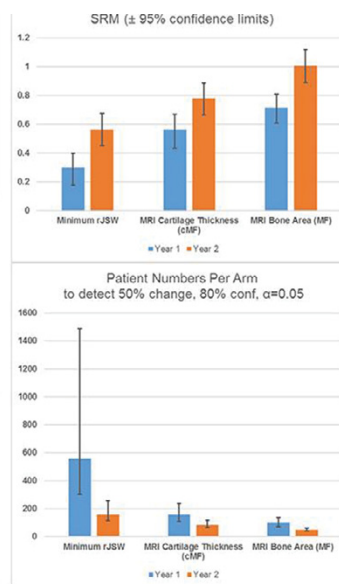
Figure 1B: Responsiveness of knees selected for JSW 2-4 and pain ≥3 (n=331)

Top figure shows SRMs plus 95% confidence limits, bottom figure calculates numbers required to identify change from SRMs in top figure

Conclusions: Selecting patients based on 2 simple criteria will improve responsiveness in clinical trials for all 3 imaging outcomes using standard imaging outcomes. Selecting for rJSW of 2–4mm is most important while adding a pain criteria further improves responsiveness; no other covariates improved this. Caution should be applied when using SRM to power a study because of the inherent difficulties in calculating standard deviations; Fig 1B shows for example that the confidence limits for rJSW at 12 months vary from 302 to 1489. This analysis also confirms the advantages of MRI outcomes over rJSW in terms of study size and duration: a 12-month study with cartilage thickness or bone area endpoints needs no more than 238 or 137 patients (including the upper 95th percentile confidence limit).

Disclosure of Interest: M. Bowes Employee of: Imorphics Ltd, G. Guillard Employee of: Imorphics Ltd, A. Brett Employee of: Imorphics Ltd, G. Vincent Employee of: Imorphics Ltd, P. Conaghan: None declared

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OP0165   **A NEOEPITOPE FRAGMENT OF C-REACTIVE PROTEIN IS PROGNOSTIC OF RADIOGRAPHIC KNEE OA**

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Background: There are two major needs in clinical development of DMOADs: 1) Identifying a suitable population with an active and progressive disease in order to demonstrate significant improvements by an efficacious intervention; and 2) Phenotyping patients and linking them to a corresponding treatment mode-of-action (e.g. anti-inflammatory). The biochemical marker CRPM is a neoepitope of C-reactive protein (CRP) and is released from the local inflamed tissue when CRP is degraded by proteases such as matrix metalloproteinases

Objectives: The purpose of this study was to translate the CRPM, from rheumatoid arthritis (RA), where it has been extensively tested, to OA, and to test whether it is predictive of radiographic OA.

Methods: The placebo arms of two phase III OA trial (clinicaltrial.gov: NCT00486434 and NCT00704847), a phase III RA study (the LITHE study, N=490), which included patients with active, moderate-severe RA (NCT00106535), as well as in an early RA cohort (N=92) were used. Subjects with symptomatic and radiographic knee OA: WOMAC pain ≥150mm and/or WOMAC function ≥510mm, and Kellgren-Lawrence grade (KLG) 2 or 3. KLG were scored for both knees at baseline and year 2 (Y2). Serum CRPM and hsCRP were measured at baseline. The association between serum CRPM levels and disease activity score (DAS28) and hsCRP was investigated by Spearman's correlations. Quartile ranges of CRPM in the early RA cohort were used to define the cut-off between inflammatory OA and non-inflammatory OA. OA knees were divided into cases and controls based on a terminology proposed by the FNIH-OAI consortium (1); knees with KLG≥2 at BL were excluded, and incidence OA at Y2 was defined KLG≥2. Logistic regression was used to compare cases and controls.

Results: There was a significant correlation between disease activity measures and CRPM in both RA studies. Seventy-five percent of the LITHE patients had high or very high levels of CRPM at BL, which was changed to a pattern similar to early RA after treatment. The mean CRPM levels were significantly lower in OA (8.5 [95% CI 8.3–8.8] ng/mL) compared to the RA patients (15.6 [9.5–21.6] ng/mL); however, a significant subset of OA patients (41% and 31% in SMC2301 and SMC2302) had CRPM levels ≥9ng/mL, as 75% of patients with early RA. Patients with BL or Y2 CRPM levels ≥9ng/mL were more likely to develop knee OA than patients with low level of CRPM. Overall, moderate to very high levels of CRPM at BL and Y2 were predictive of incidence OA with odds ratio of 4.6 [1.2–17] and 2.5 [1.2–4.8].

Table		Early RA	Moderate-Severe RA		SMC2301	SMC2302
hsCRP	Rho (p-value)	0.54 (<0.0001)	0.66 (<0.0001)			
DAS28	Rho (p-value)	0.43 (<0.0001)	0.24 (<0.0001)			
CRPM level	**Quartile range**	No. of patients (%)				
		Before treatment	After treatment	n_1	n_2	
Low	<9 ng/mL	49 (8.2%)	87 (18%)	267 (59%)	233 (69%)	
Moderate	9-12	100 (17%)	123 (25%)	137 (31%)	71 (21%)	
High	12 − 15	132 (22%)	105 (21%)	26 (6%)	23 (7%)	
Very high	>=15	318 (53%)	175 (36%)	19 (4%)	11 (3%)	

Conclusions: A subset of OA patients, up to 41%, appear to have tissue inflammation comparable to that of RA, reflected by the level of CRPM. Furthermore, high CRPM levels was prognostic of incident knee OA. These data suggest that CRPM is blood-based biochemical marker for finding OA patients with an inflammatory phenotype.

References:

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