P_32

Home monitoring of rheumatic diseases: A feasibility study to determine usage, usability and satisfaction with the ReumaMeter smartphone app

W.H. Bos[1], S. Rico[1], M. L'Ami[1], F.S. Catarinella[2], M. Boers[1], F. Turkstra[1], G. Wolbink[1], D. van Schaardenburg[1], M.T. Nurmohamed[1]

[1]Reade, Amsterdam, Netherlands, [2]Brightfish, Hoofddorp, Netherlands

Background

The use of information and communication technologies (ICT) tools for health care delivery (eHealth) empowers patients and increases their involvement in their own care process. eHealth may improve outcomes and the patient experience as well as reduce the costs. Following the Medical Research Council guidance (1) for developing and evaluating complex interventions we developed such a eHealth tool, the ReumaMeter smartphone app (see figure). It uses a validated patient reported outcome measure (PROM), the MDHAQ/RAPID3© questionnaire (2) to assess disease activity, gives direct graphical feedback of the calculated outcomes and provides information about the scores.

Objectives

To determine usage, usability and satisfaction with the ReumaMeter for home monitoring of PRO's in patients with rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA) in daily clinical practice.

Methods

A one-month feasibility study was conducted in 42 patients with RA, SpA and PsA. Feedback was provided via a survey with 47 questions. Main outcome measures were usage of >70%, a system usability score of > 70 (range 0-100) (3); overall score of ≥ 8 (0-10) and a positive net promotor score (NPS) (4). Feedback and privacy issues were also collected.

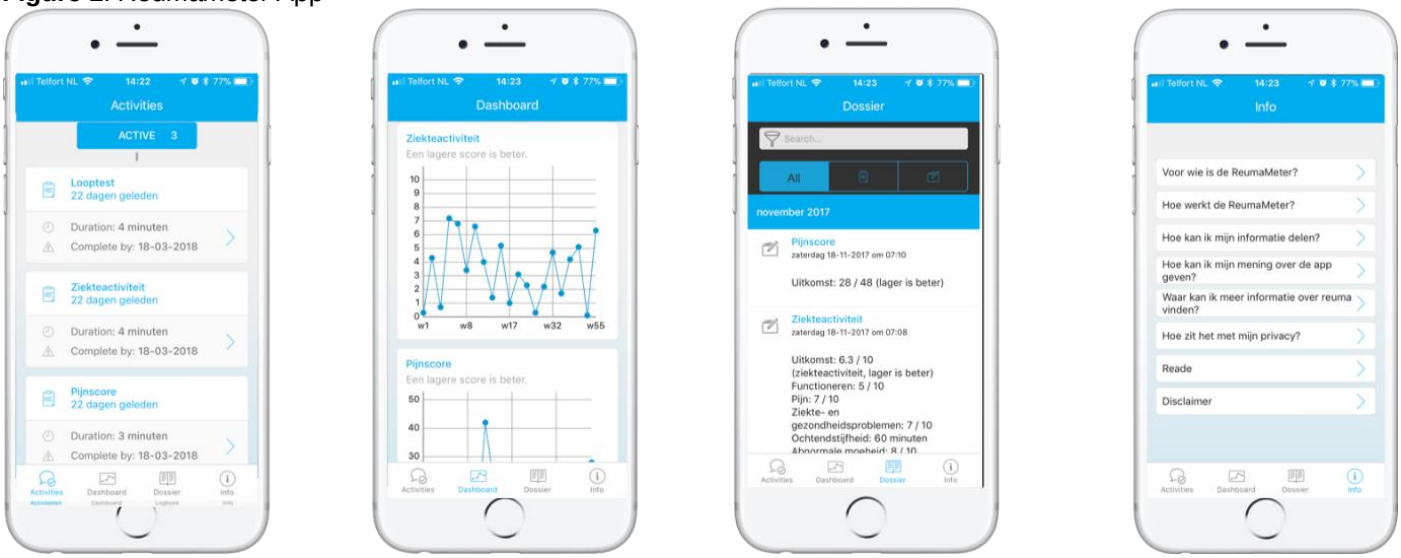
Results

Six patients could not download the app due to personal phone issues. Five patients did not return the survey, hence 31 surveys were available for analysis. Sixty percent of patients completed the weekly RAPID3 score. The usability was good with a mean system usability score of 76 (SD 15). The app was graded with an overall score of 8.0 (IQR 7.0-9.0). The NPS was a negative 9.7 (29% promotors, 32% passives, 38% detractors). In an exploratory analysis, patients scoring a 9 or 10 on the NPS (the promotors) were more likely to experience an enhanced grip on disease activity while using the ReumaMeter than those scoring a 1-6 on the NPS (the detractors). Only one patient thought the ReumaMeter was a privacy breach. Patients would like to receive reminders in the next version of the app.

Conclusion

The ReumaMeter smartphone app is feasible in terms of usability and privacy. Usage was lower than predicted, but higher than with apps in general (60% versus 43% retention after 4 weeks) (5). Satisfaction did not meet both prespecified criteria, which could be due to patients' perception on grip of disease activity while using the app. This pilot has provided a baseline measure for continuous improvement of the app together with our patients.

Figure 1: Reumameter App



P_33

Behçet's syndrome in New York and Amsterdam: evolution from probable Behçet's to ISG criteria positive Behçet's

F.G. Kerstens[1], F. Turkstra[1], C.J. Swearingen[2], Y. Yazici[2]
[1]Reade, Amsterdam, Netherlands, [2]NYU Hospital for Joint Diseases, New York City, United States of America

Introduction

Behçet's syndrome (BS) is an auto-inflammatory vasculitis, most common in countries along the ancient Silk Road. Classification of BS most often is done with the International Study Group criteria (ISG criteria)[1].
ISG criteria positivity for BS is reached when a patient has recurrent oral ulceration and any two of the following symptoms: recurrent genital ulceration, uveitis, skin lesions and pathergy positivity. Many other manifestations are reported[1]. Differences in clinical presentation can complicate classification of the diagnosis, especially in areas where the disease is low in prevalence. Some patients are classified as "probable BS". In some of these cases patients developed additional symptoms over time and met the ISG criteria in a later stage.

Objective

To describe characteristics of patients presenting with a probable diagnosis of BS in Amsterdam and New York. To study if patients who eventually met the ISG criteria differ from those who did not.

Methods

We included consecutive patients from our outpatient clinics in New York and Amsterdam classified as possible BS at enrollment. Patients fulfilling ISG criteria and patients with an alternative diagnosis at enrollment were excluded. Baseline data were evaluated retrospectively and patients were divided into two groups: those developing ISG positive ("true") BS during follow up and those who did not. Turkey, Asia, Middle and Far Eastern countries, Arabic countries and Northern Africa were considered endemic areas.
Statistical analysis was performed using SPSS, with Chi-square tests or Fisher's exact tests for categorical data and independent sample t-tests for numerical data.

Results

189 patients were included, of whom 20 were from Amsterdam. During follow up, 71 patients (37.6%) could be classified as "true" BS after a mean period of 9.4 years (± 8.3 years) after onset of symptoms. Age, gender, ethnicity, duration of symptoms at enrollment, duration of follow up as well as RAPID3 and almost all clinical manifestations at baseline were comparable for both groups. Labial ulcers and skin manifestations at enrollment were more frequently reported. Due to a large amount of missing data, we were unable to draw any significant conclusions for HLA-B*51, pathergy, erythrocyte sedimentation rate and C-reactive protein.

Conclusion

About a third of patients classified as probable Behçet's syndrome at enrollment develop new manifestations over time and can be reclassified as ISG positive BS. Based on our data, presence of skin manifestations and labial ulcers at enrollment was significantly higher in the group eventually developing a ISG criteria positive BS.

Table 1. Baseline data from all patients who were classified as probable Behçet's syndrome at enrollment

Characteristics	**All patients** (n=189)	**ISG +** (n=71)	**ISG –** (n=118)	**P-value**
Age years (SD)	34.3 (13.7)	34.1 (13.4)	34.5 (14.0)	ns
Male n (%)	46 (24.3)	13 (18.3)	33 (28.0)	ns
Duration of follow up years (SD)	3.2 (2.4)	3.3 (2.5)	3.1 (2.4)	ns
Ethnicity: endemic area n (%)	43 (22.8)	14 (19.7)	29 (24.6)	ns
RAPID3 mean score (SD)	9.8 (6.8)	9.6 (6.9)	9.9 (6.7)	ns
Duration of symptoms years (SD)	7.3 (7.8)	7.7 (7.9)	7.0 (7.8)	ns
Oral ulcers n (%)	174 (92.1)	66 (93.0)	108 (91.5)	ns
Genital ulcers n (%)	108 (57.1)	47 (66.2)	61 (51.7)	ns
- Labia	63 (33.3)	31 (43.7)	32 (27.1)	0.019
Skin disease n (%)	58 (30.7)	31 (43.7)	27 (22.9)	0.003
Eye disease n (%)	33 (17.5)	17 (23.9)	15 (12.7)	ns
Deep venous thrombosis n (%)	4 (2.1)	2 (2.8)	2 (1.7)	ns
Thrombophlebitis n (%)	5 (2.6)	2 (2.8)	3 (2.5)	ns
Central nervous system n (%)	22 (11.6)	6 (8.5)	16 (13.6)	ns
Vascular disease n (%)	7 (3.7)	1 (1.4)	6 (5.1)	ns
Pulmonary disease n (%)	3 (1.6)	0 (0)	3 (2.5)	ns
Arthritis n (%)	35 (18.6)	16 (22.5)	19 (16.1)	ns
Gastrointestinal disease n (%)	40 (21.2)	14 (19.7)	26 (22.0)	ns
Headache n (%)	12 (6.3)	5 (7.0)	7 (5.9)	ns
Epididymitis n (% of males)	3 (6.5)	0 (0)	3 (9.1)	ns

ISG +: patients who did fulfill ISG criteria after follow-up; ISG -: patients who did not fulfill ISG criteria after follow-up; SD: standard deviation; ns: not significant

P_34

Usefulness of Michigan Hand Outcomes Questionnaire (MHQ) in hand osteoarthritis

F.P.B. Kroon[1], A. Boersma[1], A. Boonen[2], S. van Beest[1], W. Damman[1], D. van der Heijde[1], F.R. Rosendaal[1], M. Kloppenburg[1]

[1]Leids Universitair Medisch Centrum, Leiden, Netherlands, [2]Maastricht University Medical Center, Maastricht, Netherlands

Background

Tools available to measure hand pain and function in hand osteoarthritis have disadvantages, being not freely available (Australian/Canadian Hand osteoarthritis Index, AUSCAN), outdated (Functional assessment In Hand osteoarthritis, FIHOA) or a single-item tool (Visual Analogue Scale, VAS). The MHQ is free to use, validated in other diseases, and has 6 scales assessing pain, function (overall function and activities of daily living [ADL]), and 3 unique domains: work performance, aesthetics, satisfaction (all range 0-100, and higher is better except for pain).

Objective

To investigate truth and discrimination of MHQ in hand osteoarthritis.

Methods

At baseline (n=383) and two-year follow-up (n=293) symptomatic hand osteoarthritis patients from the HOSTAS cohort completed questionnaires (MHQ, AUSCAN, FIHOA, VAS pain). Work status was categorized into (fulltime/part-time) employed, reduced working capacity (sick leave or partial/complete disability to work), or not in the workforce (unemployed or retired). Reduced working capacity could be due to hand osteoarthritis or other causes. Anchor questions assessed whether pain/function levels were acceptable/unacceptable, and different (worse, unchanged, improved) compared to baseline. Number of joints with deformities was assessed, and split into tertiles (<3, 3-5, >5). To appraise validity, correlation (r_s) of pain and function domains with existing instruments was evaluated. Using external anchors to categorize patients, validity of the unique domains and discrimination of all domains was visualized in cumulative probability plots (Figure).

Results

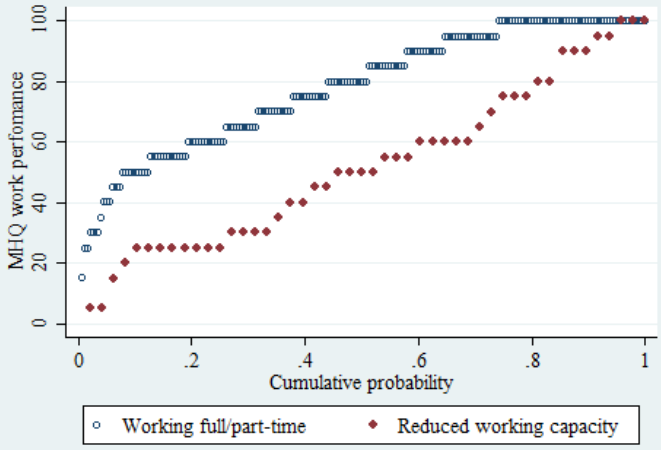
At baseline patients (84% women, median age 60.3, 90% fulfilling ACR criteria) reported moderate pain (median, interquartile range MHQ pain 45, 31.3-60) and functional impairment (MHQ overall function 57.5, 50-67.5; ADL 80.5, 68.2-89.6). MHQ pain and function scales correlated well with existing instruments (r_s=0.63-0.81). Patients with reduced working capacity had worse MHQ work performance scores than employed patients, and scores were worse if it was due to hand osteoarthritis than when there was another cause. MHQ aesthetics scores were worse in patients with more deformities. Patients with 'unacceptable' pain/function had worse MHQ satisfaction scores. All instruments measuring pain/function could discriminate between patients with acceptable vs. unacceptable pain/function, while only MHQ activities of daily living (ADL), FIHOA, and MHQ aesthetics could discriminate between erosive and non-erosive disease (not shown). MHQ and AUSCAN were most responsive (not shown).

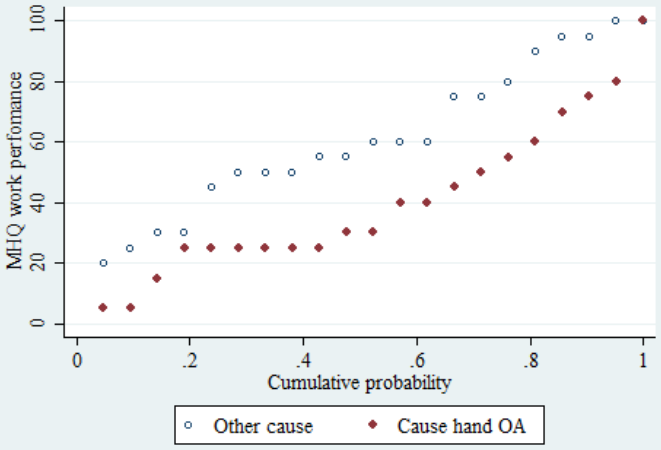
Conclusion

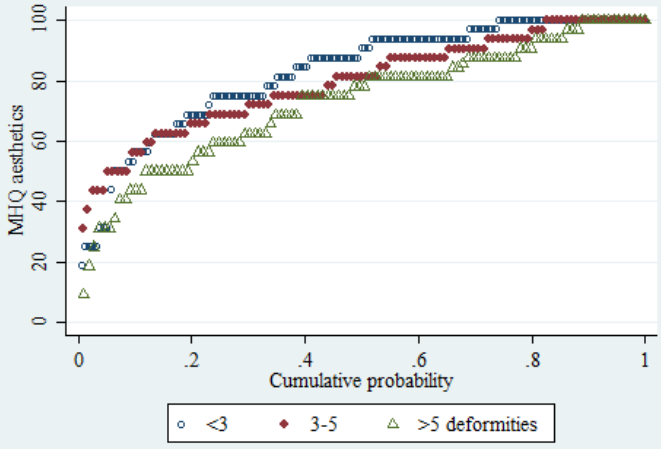
MHQ has several unique aspects and advantages justifying its use in hand osteoarthritis, including the unique assessment of work performance, aesthetics, and satisfaction. However, MHQ, AUSCAN and FIHOA appear to measure different aspects of pain and function. Assessment of sensitivity-to-change is warranted.

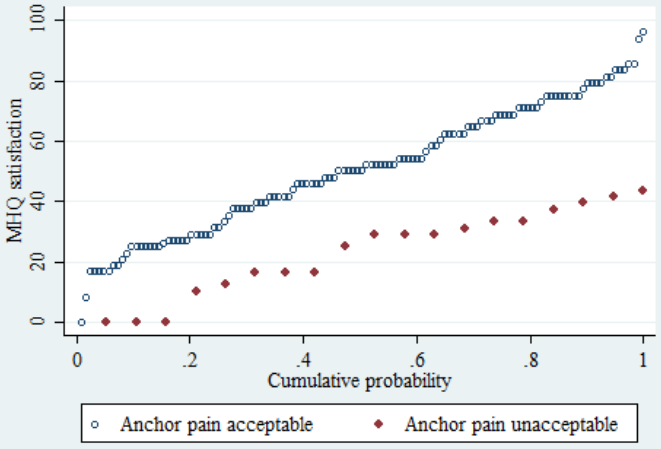
Figure 1. Exploring truthfulness of MHQ domains in cumulative probability plots

Exploring truthfulness of MHQ domains in cumulative probability plots









P_35

Disease activity in rheumatoid arthritis patients is influenced by countries' socioeconomics: results from the METEOR registry

S.A. Bergstra[1], J. Tavares-Costa[2], D. Vega-Morales[3], K. Salomon-Escoto[4], N. Govind[5], C.F. Allaart[1], R.B.M. Landewé[6]
[1]LUMC, Leiden, Netherlands, [2]Unidade Local de Saúde do Alto Minho, Ponte De Lima, Portugal, [3]Hospital Universitario Dr José Eleuterio Gonzáles, Monterrey,Mexico, [4]UMass Memorial Medical Center, Worcester,United States of America, [5]University of the Witwatersrand, Johannesburg, [6]Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands

Background
The treatment and prognosis of rheumatoid arthritis (RA) patients have improved tremendously, but patients across the world may not benefit similarly. One of the potentially critical factors may be poorer access to expensive biologic (b)DMARDs.
Objectives
To investigate daily practice data regarding bDMARD-use in different countries worldwide and assess if a lower country's socioeconomic status (SES) is associated with worse clinical outcomes and lower bDMARD-usage.
Methods
Data on disease activity and drug use from countries that contributed ≥100 RA-patients after 1-1-2000 were extracted from the daily practice, observational METEOR database. Missing data were imputed using multivariate normal imputation (30 cycles). Gross domestic product (GDP) per capita in international dollar (Intl$) was used as indicator of SES. Per country average DAS28 and the DAS28-remission percentage (DAS28<2.6) were calculated by taking the average of all patients at the last available visit. Univariable logistic regression analyses were performed to assess associations between GDP, bDMARD-use and disease outcomes at a country level.
Results
In total, 20.379 patients were included from 12 countries: United States, Mexico, South-Africa, Japan, Brazil, United Kingdom, Spain, Ireland, Portugal, France, India and the Netherlands. The number of patients ever using a bDMARD varied between 0.9% (South-Africa) and 75% (Ireland). The proportion of patients in remission at the final visit varied between 2% (India) and 39% (Netherlands).
Patients in countries with a higher GDP per capita had a lower average DAS28 and consequently, a higher proportion of them were in DAS28-remission: -0.32 (95% CI -0.41; -0.021) lower DAS28 and an additional 4.2% (0.14; 8.26) of patients in DAS28-remission for every 10.000 Intl$ additional GDP.
To underscore the assumption that the association between SES and DAS28 is mediated by bDMARD-use, we assessed whether SES was associated with bDMARD-use per country. Indeed, a higher GDP per capita was associated with a higher proportion of patients using a bDMARD: 11.2% (95% CI 4.82; 17.5) more patients using a bDMARD per 10.000 Intl$ additional GDP. Furthermore, DAS28 was -0.14 (-0.28; -0.0054) lower and 2.8% (-0.13; 5.8) more patients achieved DAS28-remission per 10% increase in proportion of patients using a bDMARD, figure 1.
Conclusions
RA-patients in countries with a lower SES had worse disease activity. Although patients in countries with a lower SES less often used bDMARDs, the effect of bDMARD use on disease activity was smaller than expected, indicating that other factors than access to bDMARDs may contribute to the effectiveness of RA-treatment.

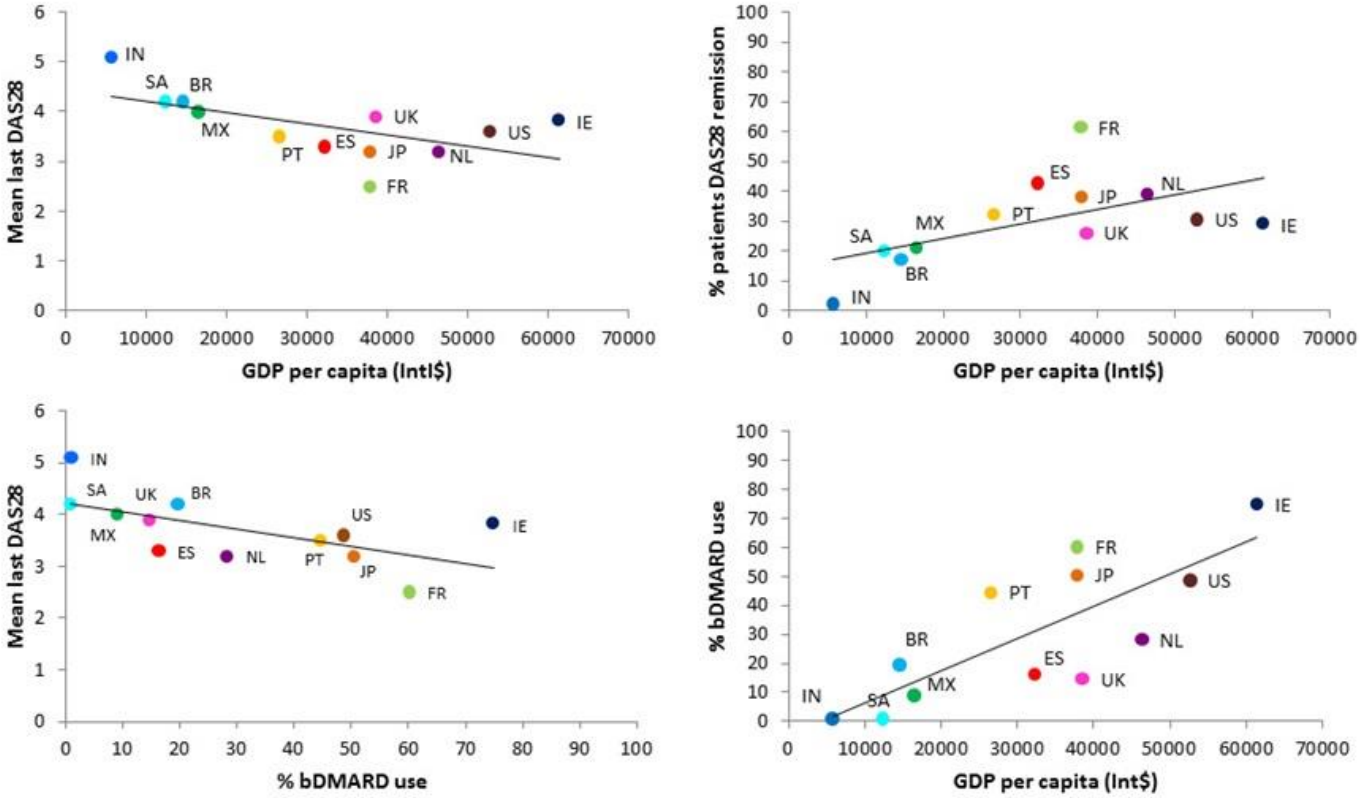


Figure 1. Associations between 'GDP per capita (IntI$), '% bDMARD use' and 'disease activity'. IN=India, SA=South-Africa, BR=Brazil, MX=Mexico, PT=Portugal, ES=Spain, JP=Japan, UK=United Kingdom, FR=France, NL=Netherlands, US=United States, IE=Ireland

P_36

How to Optimize Exercise Behaviour in Axial Spondyloarthritis: Results of an Intervention Mapping Study

S. Hilberdink[1], S.F.E. van Weely[1], F.J. van der Giesen[1], M. Nijkamp[2], N. Lopuhaä[3], T.P.M. Vliet Vlieland[1]
[1]LUMC, Leiden, Netherlands, [2]Open Universiteit, Heerlen, Netherlands, [3]Reumafonds, Amsterdam, Netherlands

Background

Regular exercise has many health benefits for people with axial spondyloarthritis (axSpA) [1]. However, most patients do not engage in frequent exercise [2]. In order to improve exercise behaviour of axSpA patients, a well-founded intervention is needed.

Objectives

To identify effective intervention methods to optimize exercise behaviour in axSpA.

Methods

The first three steps of the Intervention Mapping (IM) protocol, which is a six-step framework for intervention development, were used to determine effective intervention components. This study comprised 1) a needs assessment, to examine the discrepancy between current and desired exercise behaviour of axSpA patients, 2) a determinant analysis, to identify barriers and facilitators (determinants) to overcome this discrepancy, and 3) an intervention method analysis, to select effective methods that target these determinants. All three steps included literature reviews: PubMed and Web of Science were systemically searched for articles up to August 2017 using a well-defined search strategy. Additionally, semi-structured interviews with axSpA patients (n=2) and specialised physiotherapists (n=2) explored the literature search findings of IM steps 1 to 3 qualitatively and ranked the determinants and methods identified in steps 2 and 3 in order of relevance.

Results

The literature searches resulted in 28 (64), 23 (257) and 15 (209) included articles (hits) for IM steps 1, 2 and 3, respectively. IM step 1 revealed that only one third of axSpA patients engage in (frequent) mobility, strengthening and/or cardiorespiratory exercises, while especially these components appear beneficial in axSpA. IM step 2 showed that self-efficacy, attitude, skills, therapists' skills, knowledge, intentions, planning and exercise group support positively influence exercise behaviour in axSpA (ordered by relevance). IM step 3 identified effective methods to stimulate exercise behaviour in axSpA by targeting aforementioned determinants: guided practice, action planning, goal setting, education (on disease, coping, exercise and available resources), feedback, tailoring, motivational interviewing, monitoring, therapists' education and encouragement of exercising in a group (ordered by relevance).

Conclusions

This study showed that in order to optimize exercise behaviour in axSpA, patients should be offered an intervention including education, motivational interviewing, goal setting and action planning and they should be stimulated to exercise in a group. In addition, therapists should be educated how to tailor, practice and monitor exercise and how to base this on thorough assessment.

P_37

Cost-effectiveness of tapering TNF blockers versus conventional synthetic DMARDs in Rheumatoid Arthritis: first year results of the randomised controlled TARA-study

E. van Mulligen[1], A.E.A.M. Weel[2], T.M. Kuijper[2], J.J. Luime[1], J.M.W. Hazes[1], P.H.P. de Jong[1]
[1]Erasmus MC, Rotterdam, Netherlands, [2]Maasstad Ziekenhuis, Rotterdam, Netherlands

Background
Currently, guidelines recommend tapering treatment in rheumatoid arthritis (RA) patients who are in sustained remission. Benefits of tapering are a decreased risk of long-term adverse events and a reduction of health care costs, especially when anti-TNF is tapered. However, tapering treatment may lead to more transient or persistent disease flares, which have a direct impact on patients' lives and societal costs.

Objective
The aim of this study is to evaluate the cost-effectiveness of tapering csDMARDs or anti-TNF therapy during one year of follow-up.

Methods
The TARA trial is a multicenter single-blinded randomised controlled trial. Included were RA patients that used a combination of csDMARDs and anti-TNF and who were at least for 3 months in sustained remission, defined as a DAS≤2.4 and a swollen joint count (SJC)≤1. Patients were randomised into gradual tapering csDMARDs followed by anti-TNF or vice versa. Medication was gradually tapered by cutting the dosage into half, a quarter and after 6 months it was stopped. Data on QALYs (measured with the Dutch EuroQol [EQ5D]), direct, and indirect costs were used to calculate the Incremental Cost Effectiveness Ratio (ICER). Direct costs comprises costs for treatment and medical consumption, while indirect costs comprises costs due to loss of productivity (i.e. sick leave and unemployment).

Results
A total of 187 patients were randomly assigned to tapering csDMARDs (n=94) or tapering anti-TNF (n=95). Patients had an average symptom duration of 6.7 years and were predominantly female (66%) with an average age of 56.6 years (Figure 1A). Average QALYs (SD), over 1 year, for tapering csDMARDs or anti-TNF were, respectively, 0.82(0.1) and 0.83(0.1) (Figure 1B). One year after inclusion a none significant difference in cumulative flare ratio of 9% was observed (overall flare ratio 36%). Patients in the anti-TNF tapering group had lower costs per QALY (SD) (€11390 (6809)) compared to patients in the csDMARD tapering group (€21804 (8329)). The difference in costs per QALY were mainly determined by the medication costs (Figure 1B). The Incremental Cost Effectiveness Ratio (ICER,95% CI) between tapering csDMARDs and anti-TNF was €31922 (-€920572,€984416) (Figure 1C). Tapering anti-TNF was >95% cost-effective across all willingness-to-pay thresholds compared to tapering csDMARDs (Figure 1D).

Conclusion
Tapering anti-TNF is more cost-effective compared to tapering csDMARDs. Therefore, in RA patients who are in sustained remission we advise to taper anti-TNF first, but before tapering therapy rheumatologists should take the risk of a disease flare and patient's wishes into account.

A

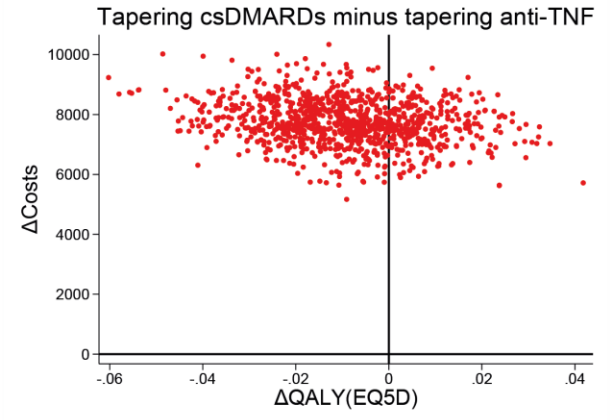
	Tapering csDMARDs	Tapering anti-TNF
Baseline (t=0)		
Age (yrs), mean (SD)	55.9 (14)	57.2 (11)
Gender, female, n (%)	67 (71)	58 (61)
Symptom duration (yrs), median (IQR)	5.9 (4.3-8.5)	6.3 (4.1-8.9)
RF positive, n (%)	50 (57)	56 (64)
ACPA positive, n (%)	62 (72)	65 (75)
DAS, mean (SD)	1.1 (0.6)	1.0 (0.5)
DAS remission, DAS44<1.6, n (%)	76 (81)	84 (88)
HAQ, mean (SD)	0.52 (0.47)	0.45 (0.48)
1-year follow up (t=12)		
DAS, mean (SD)	1.31 (0.64)	1.35 (0.75)
DAS remission, DAS44<1.6, n (%)	57 (69)	58 (66)
Cumulative flare, n (%)	30 (35)	40 (45)
HAQ, mean (SD)	0.59 (0.62)	0.56 (0.56)

B

	Tapering csDMARDs	Tapering anti-TNF
QALYs (AUC)	0.82 (0.1)	0.83 (0.1)
Cost per QALY (EQ5D)		
Total direct costs, €*	20718 (6898)	11124 (6439)
• Medication, €*	19137 (5943)	9275 (5202)
• Medical consumption, €	1304 (1216)	1314 (1066)
• Hospitalization, €	278 (1675)	534 (3115)
Total indirect costs, €	1082 (4071)	267 (2985)
Total costs per QALY, €*	21804 (8329)	11390 (6809)

Results shown are mean (SD). *P<0.001 (Student's *t* test).

C



D

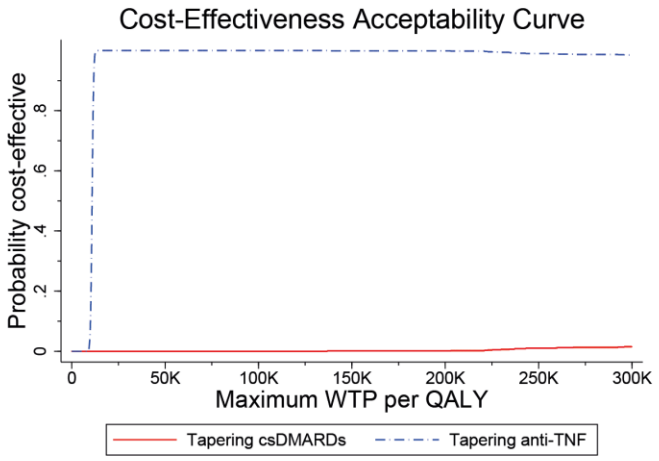


Figure 1 Summary of economic evaluation. (A) Baseline characteristics and results after 12 months of follow-up of both tapering groups. (B) Total costs per QALY after 1 year of follow-up. (C) Cost effectiveness plane of costs of tapering csDMARDS minus costs for tapering anti-TNF. (D) Cost-acceptability curves for tapering csDMARDs and tapering anti-TNF. Abbreviations: AUC; area under the curve, csDMARDs; conventional synthetic DMARDs, EQ-5D; Dutch EuroQol, QALY; quality adjusted life year, WTP; willingness to pay.

P_38

The patients' perspectives towards the provision of information during transition to a biosimilar

Z. Layegh[1], J. Kreuk[2], A. Twisk[2], J. Meilink[2], R. Alblas[2], W. Van der Weele[2], R. c.f Hebing[3], J. Ruwaard[2], M. j L`Ami[2], G. Wolbink[2]

[1]Amsterdam Rheumatology and immunology Center | Reade, Amsterdam, Netherlands, [2]Rheumatology and immunology Center | Reade, Amsterdam, Netherlands, [3]Reade, Rheumatology, Pharmacy. Amsterdam, Amsterdam,Netherlands

Background

In July 2015, at the Amsterdam Rheumatology and Immunology Centre, location Reade, 93% of the patients with rheumatoid arthritis, treated with reference product infliximab switched to the biosimilar infliximab. This transition was needed to enable cost savings. Patients gained information via several ways, where the rheumatology nurses had a central role in informing the patients. Patients' perspectives are warranted to investigate the effect of the transition to the biosimilar.

Objectives

To investigate patients perspectives towards the provided information regarding the switch to the biosimilar.

Methods

Consecutive patients treated with reference product infliximab were switched to the biosimilar in the period July 2015 to June 2016 at the Amsterdam Rheumatology and immunology Center, Reade. Patients were informed by a letter about the transition to the biosimilar and were subsequently contacted by a nurse or the pharmacist for additional questions and whether they agreed upon the switch. All patients who were switched from the reference product to the biosimilar were approached at the day care to fill in a questionnaire. In this qualitative questionnaire, patients were asked to evaluate the information provision process and how they gained information about the transition to the biosimilar initially. This was done by the nurses of the day care.

Results

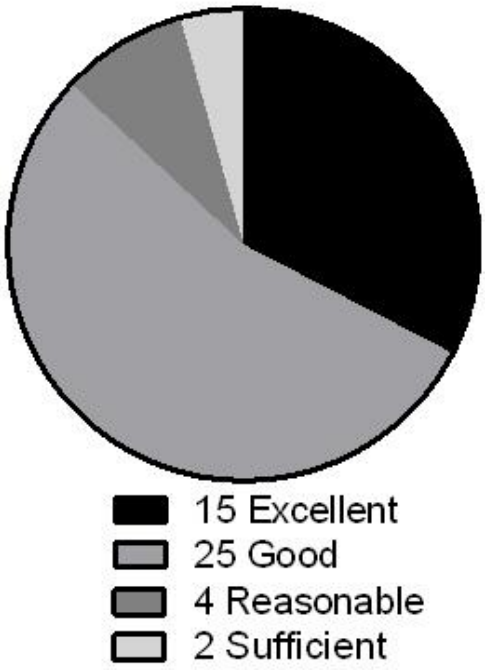
All patients who switched to the biosimilar (n=46) filled in the questionnaire, of which 15 patients scored the information provision as excellent (33%), 25 patients as good (54%), 4 patients as reasonable (9%) and 2 patients found the information sufficient (4%). Furthermore, the majority of patients was initially informed by nurses and rheumatologist prior to the letter that was send to all patients. In total, 12 patients were initially informed by rheumatology nurse (26%), 12 patients by the rheumatologist (26%). Four patients were informed via the letter that was send at first (9%) and 3 patients gained the information about the transition otherwise (7%). Fifteen patients gave more than one answer to the question by whom they were informed initially.

Conclusions

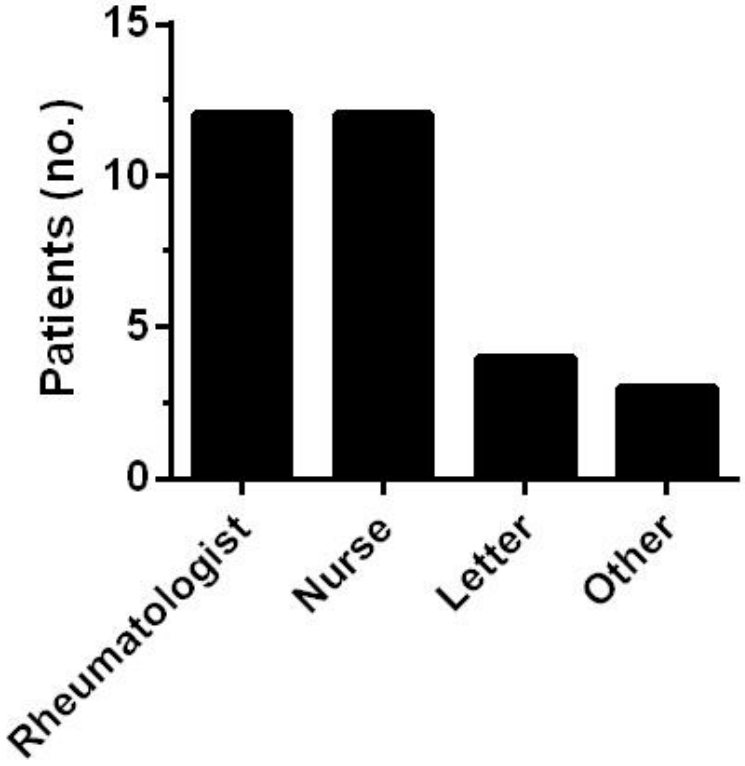
Patients were satisfied about the information provision process, there were no patients who experienced the information provision insufficient. Next to the rheumatologist, rheumatology nurses played an important role in informing the patients about the transition.

Figure 1: A. Patients perspective towards the information provision about the transition to the biosimilar. B. Patients initially informed about the biosimilar.

A. Patient's perspective



B. Initially informed by:



P_39

Hepatitis C gerelateerde artritis

E.H.C.C. Janssen, J.G.M. Koeleman, D. van Zeben
Franciscus Gasthuis, Rotterdam, Netherlands

Introductie / Achtergrond

Wereldwijd zijn er 170 miljoen mensen met antistoffen tegen het hepatitis C virus (HCV) en 130 miljoen mensen zijn chronisch drager van het virus (in Nederland 28.000). De mortaliteit bedraagt 700.000 per jaar. Sinds 2015 zijn de zgn. DAA (direct acting agents) voor elke HCV patiënt in Nederland beschikbaar. De sustained virological respons van deze middelen is hoog.[1]

Naast de hepatische problemen kan HCV ook extra-hepatische verschijnselen geven. De meest gerapporteerde klacht is musculoskeletaal. Ook artritis in het kader van HCV wordt beschreven in 2-4% van de gevallen. Er zijn twee klinische verschijningsvormen: een mono- of oligoartritis (vaak in het kader van cryoglobulinemie) en een polyartritis met een zelfde verdeling zoals bij reumatoïde artritis (RA), waarbij IgM reumafactor ook vaak positief is. Het kan dan ook lastig zijn het onderscheid te maken.[2,3]

Doel van de studie

Epidemiologische cijfers over HCV-gerelateerde artritis wisselen erg per land. El Garf et al. publiceerden in 2011 hun opnamecijfers op de afdeling reumatologie in Caïro: 11% was HCV gerelateerd.[4] In Frankrijk werden 233 patiënten met een polyartritis gescreend op HCV: slechts 1 patiënt bleek positief.[5] Getallen uit Netherlands ontbreken.

Methode en Resultaten

In het Franciscus Gasthuis is gekeken hoe vaak de diagnose HCV-gerelateerde artritis werd gesteld. In de periode januari 2010 tot juli 2016 werd HCV-serologie door alle specialismen tezamen 14.614 keer aangevraagd; 191 patiënten bleken positief (1.3%). Er was dossierinzage bij 132 patiënten. De mediane leeftijd bedroeg 58 (26-96) jaar en 55.3% was man. De helft van de patiënten was afkomstig uit Netherlands. Ruim een kwart had normale levertesten en HCV-PCR, indien verricht, bleek in 65.7% positief. Van deze patiënten had 12.3% ook een inflammatoire gewrichtsziekte (spondylartropathie, jicht, RA, poly- en monoartritis n.n.o.).

De diagnose HCV-gerelateerde artritis werd één keer gesteld. Deze patiënt was volledig klachtenvrij na succesvolle antivirale behandeling. Er waren daarnaast twee patiënten met artralgieën o.b.v. HCV. Wat het effect van antivirale behandeling op hun gewrichtsklachten was, is onbekend.

Discussie en Conclusie

De diagnose HCV-gerelateerde artritis en/of artralgieën werd in de periode 2010 – juli 2016 drie keer gesteld. Of dit te maken heeft met unawareness of met een lage prevalentie van het ziektebeeld, komt in dit retrospectieve onderzoek niet naar voren en vereist verder prospectief onderzoek.

P_40

Rheumatoid arthritis (RA)-associated autoantibodies are present in the periodontal exudate of patients with and without RA

J. Westra[1], P.S. Rahajoe[2], M.J. de Smit[1], G.J. Schuurmans[1], E. Eelsing[1], N. Kertia[2], A. Vissink[1]
[1]UMCG, Groningen, Netherlands, [2]Dr. Sardjito General Hospital, Yogyakarta, Indonesia

Background
Seropositivity for anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) is a hallmark of RA and can be present years before clinical onset has become apparent. Environmental factors, including smoking and chronic inflamed mucosal tissues of the lungs, gastro-intestinal tract or oral cavity (i.e. the periodontium), are suggested to contribute to initiation of these autoantibodies. While it is known that the inflamed periodontium contains citrullinated proteins and peptides, only Harvey et al. (2013) showed that IgG ACPA is indeed present in the periodontal exudate (n=9).
Objectives
As the IgA isotype is specific for mucosal immunity, we assessed in patients with and without RA whether IgA RF and IgA ACPA are present gingivocrevicular fluid (GCF), the periodontal inflammatory exudate.
Methods
RA patients fulfilling the ACR/EULAR 2010 classification criteria were recruited at the Rheumatology department of the Dr. Sardjito General Hospital, Yogyakarta, Indonesia. Patients without RA (non-RA) were recruited from the Oral Surgery department of the same hospital. Patients with diabetes or cardiovascular disease were excluded. Periodontitis was defined as periodontal inflamed surface area (PISA)>130 mm^2 (Leira et al. 2017). RF and ACPA were determined by ELISA in serum (IgM RF, IgA RF, IgG ACPA, IgA ACPA) and GCF (IgA RF, IgA ACPA). In addition, total IgA and IgG were determined in GCF. IgA ACPA seropositivity and IgA RF- and IgA ACPA positivity in GCF were defined as >mean+2SD of healthy controls (non-RA patients, never smokers, no periodontitis, n=88).
Results
In non-RA patients (n=151), PISA was correlated with total IgG and IgA in GCF ($p<0.0001$). IgA RF and IgA ACPA were present in GCF and correlated with total IgA in GCF ($p<0.05$ and $p<0.01$ respectively). In contrast to RA patients (n=72), IgA RF and IgA ACPA in GCF of non-RA patients were not correlated with IgA RF en IgA ACPA in serum. In non-RA patients, IgA ACPA positivity in GCF was more frequent in ever smokers (18%) than in never smokers (9.8%), the same held for presence or absence of periodontitis (18 and 9.3% IgA ACPA positivity in GCF respectively). Moreover, in non-RA patients PISA was correlated with IgA ACPA in serum ($p<0.01$) and GCF ($p=0.05$).
Conclusions
RA-associated autoantibodies are present in GCF, and are presumably the result of local formation due to periodontitis.

P_41

How do spondyloarthritis patients perceive quality of care in daily practice?

E.A.B. Beckers, Y. van Eijk - Hustings, A. Boonen, A. van Tubergen
Maastricht University, Maastricht, Netherlands

Background
Assessing the patient's perspective on quality of care is important for quality improvement. For this purpose patient reported experience measures (PREMs) have been developed and validated. Currently, it is unknown how spondyloarthritis patients experience quality of care in daily practice in the Netherlands.

Objectives
To assess how patients with spondyloarthritis perceive the quality of care provided in daily practice in an academic rheumatology department.

Methods
A heterogeneous sample of patients with spondyloarthritis was recruited from the rheumatology department, Maastricht UMC+. Perceived quality of care of the past year in daily practice for these patients was assessed by a validated patient reported experience measure for rheumatic conditions (PREM) and by semi-structured focus group interviews (1). Domains in the PREM were needs and preferences; coordination and communication; information-, instruction and self-care; daily life and physical comfort; emotional support; family and friends; access to care and overall experience with care. Interviews explored in more depth practical care aspects and patients were asked to elaborate on their perceived care experiences. Questionnaire results were analyzed descriptively and interviews were audiotaped and analyzed in NVIVO11 software.

Results
Sixteen patients with spondyloartritis completed the PREM and participated in four focus group interviews. Mean age was 62 years (range 41-77 years), 10 were female (62.5%) and average time since diagnoses was 28 years.
PREM results showed that patients felt respectfully treated by their care provider and they received information in an understandable way. Patients were less satisfied with information received about patient organizations and most of them felt that they had not received the opportunity to participate in self-management programs.
Interviews further clarified that patients in general were satisfied with care in daily practice in the previous year. Patients were very satisfied with appointments in time and the duration of consultations. Patients underlined the importance of a personal patient – care provider relationship and the need to make comprehensive notes in case a colleague takes over. Although access to the nurse telephone helpline was considered adequate, there was room for improvement.

Conclusions
Patients with spondyloartritis mentioned a number of points for improvement for a rheumatology department in the Netherlands. Aspects mentioned were quality of advice of the nurse telephone line, and providing patients with information about patient organizations and self-management programs.

P_42

Systematic review for the 2018 update of the EULAR management recommendations for hand osteoarthritis

F.P.B. Kroon[1], M. Kloppenburg[1], J.W. Schoones[1], L. Carmona[2]
[1]Leids Universitair Medisch Centrum, Leiden, Netherlands, [2]Instituto de Salud Musculoesquelética, Madrid, Spain

Background
The EULAR management recommendations for the management of hand osteoarthritis (OA) were issued in 2007 and needed an update.
Objectives
To inform the task force of available evidence for the efficacy and safety of all non-pharmacological, pharmacological and surgical interventions for hand OA.
Methods
A systematic review of available evidence for hand OA treatment was performed. We searched Medline, EMBASE, Cochrane Central, and 2016-2017 conference abstracts until June 2017 for (randomised) controlled trials or Cochrane reviews. Observational studies with a comparator were included to assess safety, or effects of surgical interventions. Main efficacy outcomes were pain, function, and hand strength. Risk of bias was assessed. Meta-analysis was performed if possible.
Results
Of 7,036 records, 127 references were included, of which 50 studies concerned non-pharmacological, 64 concerned pharmacological, and 12 concerned surgical interventions. Most trials were published after 2007. Many studies were at high risk of bias, mainly due to inadequate randomisation or lack of blinding. Overall, effect sizes of effective therapies were small. Beneficial non-pharmacological treatments for pain relief include hand exercise, and prolonged splinting of the thumb base. A single trial showed that assistive devices had no effect on pain, but led to functional improvements (mean difference (MD) -0.3, 95% confidence interval (CI) -0.6; 0.01 on AUSCAN function, range 1-5). Topical and oral non-steroidal anti-inflammatory drugs (NSAIDs) proved equally effective for pain relief, while topical NSAIDs led to less adverse events (e.g., risk ratio for withdrawals due to adverse events 0.15, 95% CI 0.03; 0.63). Single trials demonstrated beneficial effects for other pharmacological interventions, including chondroitin sulphate, and intra-articular (i.a.) glucocorticoid injections in interphalangeal joints. Compared to placebo, no beneficial effects were demonstrated for i.a. glucocorticoid or hyaluronic acid injections in the thumb base, hydroxychloroquine, or tumor necrosis factor inhibitors. In two trials, structure modification was the primary outcome measure, though no disease-modifying properties were found in these studies. In a Cochrane review no surgical intervention for thumb base OA appeared more effective than another, although in general, more complex procedures led to more complications.
Conclusions
The number of trials in hand OA has steeply increased over the last decade, providing evidence for several therapeutic options for symptom relief, though no disease-modifying drugs have yet been found. High-quality trials investigating often used analgesics like paracetamol are needed.

Table 1. Effect on pain of main non-surgical interventions for hand osteoarthritis (OA) from controlled trials

Table. Effect on pain of main non-surgical interventions for hand osteoarthritis (OA) from controlled trials

Intervention	Control	N patients (studies)	Duration	OA type or location	RoB	Difference?	Effect estimate [95% CI]
Non-pharmacological interventions							
Hand exercise	No exercise	381 (5)	12 w	-	High	Intervention better	SMD -0.27 [-0.47;-0.07]
Joint protection	No joint protection	257 (1)	26 w	-	High	No	MD -0.79 (-1.7;0.12) on AUSCAN pain (range 0-20)
Thumb splint	Usual care or no intervention	221 (4)	4-8 w	CMC	High	No	MD -2.9 [-12.2;6.5] on 100 mm VAS
		137 (2)	13-52 w	CMC	High	Intervention better	MD -17.4 [-25.6;-9.2] on 100 mm VAS
Long thumb splint (MCP + CMC joint)	Short thumb splint (only CMC joint)	185 (3)	2-12 w	CMC	High	No	MD -0.85 [-5.1;3.4] on 100 mm VAS
DIP splint	No intervention	26 (1)	12 w	DIP	High	No	Median difference -0.5 [range -7;3.5, p-value 0.53] on 10 cm VAS
Assistive devices	Information provision	70 (1)	12 w	-	High	No	MD 0.4 [-9.8;10.6] on 100 mm VAS
Pharmacological interventions							
Topical NSAID	Topical placebo	385 (1)	8 w	-	Low	Intervention better	MD -5.9 [-11.7;-0.06] on 100mm VAS
Topical NSAID	Oral NSAID	381 (2)	3 w	"activated" IP OA	Low	No	SMD -0.05 [-0.27;0.17] (1 trial, n=321)
Oral NSAID	Placebo	695 (3)	2-4 w	-	Low	Intervention better	SMD 0.40 [0.20;0.60] (2 trials, n=654)
Chondroitin sulphate	Placebo	162 (1)	26 w	-	Low	Intervention better	MD -8.7 [p=0.016] on 100mm VAS
i.a. glucocorticoids	i.a. placebo	206 (3)	26 w	CMC	Low/unclear	No	MD -3.6 [-13.9;6.8] on 100mm VAS (2 trials, n=166)
i.a. glucocorticoids	i.a. placebo	60 (1)	12 w	IP	Low	Intervention better	MD -18.0 [-33.5;-2.6] on 100mm VAS
i.a. hyaluronic acid	i.a. placebo	235 (3)	26 w	CMC	Unclear	No	MD 3.3 [-5.2;11.8] on 100mm VAS (1 trial, n=123)
Hydroxychloroquine	Placebo	503 (3)	24-52 w	-	Unclear	No	MD 2.9 [-3.4;9.2] on 100mm VAS (2 trials, n=307)
TNF inhibitor	Placebo	235 (3)	24-52 w	Erosive OA	Low	No	MD -4.9 [-12.5;2.8] on 100mm VAS (2 trials, n=175)

AUSCAN, Australian/Canadian hand osteoarthritis index; CI, confidence interval; cm, centimetre; CMC, first carpometacarpal; DIP, distal interphalangeal joint; i.a., intra-articular; MCP, metacarpophalangeal joint; MD, mean difference; mm, millimetre; NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; OR, odds ratio; RoB, risk of bias; RR, risk ratio; SMD, standardized mean difference; TNF, tumor necrosis factor; VAS, visual analogue scale; w, week(s).

P_43

Rapid and sustained effect of filgotinib, an oral JAK1 selective inhibitor, on patient-reported outcomes : Results from a Phase 2B dose-ranging study in active RA patients

C.F. Allaart[1], L. Meuleners[2], C. Tasset[2], P. Harrison[2], A. van der Aa[2], R. Westhovens[3]
[1]Leiden University Medical Center, Leiden, Netherlands, [2]Galapagos NV, Mechelen, Belgium, [3]University Hospitals Leuven, Leuven, Belgium

Background
Filgotinib is a next-generation, oral, selective JAK1 inhibitor that has shown efficacy and safety both as add-on to methotrexate (MTX) and as monotherapy in two 24-week (wk) placebo-controlled Phase 2B studies in patients with active rheumatoid arthritis (RA) and an inadequate response to MTX.
Objective
To investigate the effect on patient-reported outcomes (PROs) of filgotinib as add-on to MTX in patients with active RA.
Methods
Patients with active RA on a stable dose of MTX were randomized in a double-blinded manner to placebo (PBO) or one of three total daily doses of filgotinib (50mg, 100mg, 200mg) and two regimens (qd and bid) for 24 wks. PROs measured were patient's global disease assessment and pain, physical function (HAQ-DI), fatigue (FACIT-F) and HRQoL-SF-36 mental/physical component scores (MCS/PCS). Results are presented from patients dosed with filgotinib 100mg or 200mg qd (selected Phase 3 doses) or PBO.
Results
594 patients were randomized and dosed. Baseline mean DAS28(CRP) was 6.1 and mean HAQ-DI was 1.7, indicating significant disease burden. Both doses of filgotinib showed rapid statistically significant improvement in PROs compared to PBO: 200mg qd showed statistically significant effects as early as wk 1 for patient global disease assessment, wk 2 for patient pain and HAQ-DI, and wk 4 (earliest timepoint measured) for FACIT-F and SF-36 PCS. With 100mg qd, patient global disease assessment, patient pain and HAQ-DI significantly improved as of wk 2; and FACIT and SF-36 (PCS and MCS) as of wk 4. At wk 12, in both the 100mg qd and 200mg qd dosing groups, a higher proportion of patients showed normalized values for HAQ-DI, FACIT and SF-36 PCS and MCS compared to PBO. Responses were maintained or continued to improve throughout 24 wk dosing.
Conclusion
Filgotinib 100mg and 200mg qd, as add-on treatment to MTX, led to early symptomatic relief as demonstrated by significant improvement in PROs as of the first timepoints measured; this effect was sustained.

P_44

Are older rheumatoid arthritis patients frail, or lonely and depressed?

F.A.H.M. Cleutjens[1], A. Boonen[2], M.G.B. van Onna[2]
[1]Maastricht University, Maastricht, Netherlands, [2]MUMC+, Maastricht, Netherlands,

Background
The average rheumatoid arthritis (RA) patient has approximately two comorbidities, and this number increases with age. Both comorbidity and aging are considered risk factors for frailty, a physiological syndrome characterized by reduced functional reserves and resistance to 'stressors' due to a cumulative decline of physiological and psychosocial systems. Frailty results in adverse health outcomes including hospitalization and increased risk of mortality. The extent to which frailty is a relevant problem in elderly RA patients remains unknown.

Objectives
(1) To assess the prevalence of frailty and (2) to identify which factors are associated with frailty in elderly patients with RA.

Methods
Consecutive patients of the outpatient clinic where invited to participate in a study on aging while ensuring equal representation of patients in three pre-defined age groups: 55-64, 65-74, and ≥75 years. Rheumatologists recorded the number of comorbidities. Patients rated their overall health on a visual analogue scale (0-100; 100 very bad health) and completed the validated Groningen Frailty Indicator (GFI), which contains 15 questions on the loss of functions and resources across four domains: physical (mobility functions, multiple health problems, physical fatigue, vision, hearing), cognitive (cognitive dysfunction), social (emotional isolation), and psychological (depressed mood and feelings of anxiety). Scores on items are dichotomized, '1'; indicating a problem or dependency. Prevalence of problems/dependency was compared among the three age-groups using a Kruskal-Wallis test. Characteristics of patients classified as frail (GFI score ≥4) or non-frail (GFI score <4) were compared using a chi-square test for categorical data or the independent samples t-test for continuous data.

Results
The prevalence of frailty across age groups was respectively 43.3%. 40.0% and 43.4%. Frail RA patients were more often female, had a lower subjective health status. Remarkable, patients classified as frail identified problems in the social and psychosocial domains. Of interest, there were no differences regarding age, polypharmacy, number of comorbidities, and cognitive domain (Figure 1).

Conclusion
Using validated questionnaires, frailty is highly prevalent in all RA patients older than 55 years and seems to be a distinctive health construct which is not necessarily related to increasing age, polypharmacy and comorbidity in patients with RA. An alternative explanation of our findings is that rheumatologists seem to miss symptoms of depression and loneliness among RA patients.

Table 1: Demographics, clinical characteristics, and number of patients with problems/dependency per frailty domain in frail and non-frail elderly RA patients

Table: Comparison of demographics, clinical characteristics, and number of patients with problems/dependency per frailty domain between frail and non-frail elderly rheumatoid arthritis patients.

	Frail (n=38)	Non-frail (n=52)	p-value
DEMOGRAPHICAL CHARACTERISTICS			
Male	8 (21)	22 (42)	0.035
Age, mean (SD)	69.9 (9)	69.6 (7)	0.878
CLINICAL CHARACTERISTICS			
Patient global health (0-100), mean (SD)	45.7 (20)	34.5 (16)	0.004
Comorbidities, mean number (SD)	0.6 (1)	0.5 (1)	0.862
FRAILTY DOMAIN SCORES			
Physical domain GFI; problem or dependency: n (%)			
Grocery shopping	5 (13)	2 (4)	0.103
Walk outside the house	3 (8)	0 (0)	0.039
Getting (un)dressed	2 (5)	0 (0)	0.094
Visiting restroom	1 (3)	0 (0)	0.239
Vision	5 (13)	2 (4)	0.103
Hearing	6 (16)	6 (12)	0.558
Nutrition	6 (16)	1 (2)	0.015
Use of 4≥ medication types	30 (79)	38 (73)	0.522
Subjective physical fitness	23 (61)	13 (25)	0.001
Cognitive domain GFI; problem or dependency: n (%)			
Memory complaints	10 (26)	6 (12)	0.070
Social domain GFI; problem or dependency: n (%)			
Emptiness	24 (63)	2 (4)	<0.001
Missing the presence of people around	25 (66)	4 (8)	<0.001
Feelings of loneliness	21 (55)	0 (0)	<0.001
Psychosocial domain GFI; problem or dependency: n (%)			
Feelings of depression	28 (74)	6 (12)	<0.001
Nervous or anxious feelings	22 (58)	8 (15)	<0.001

Data are presented as number (percentage) of patients unless stated otherwise.

P_45

The clinical profile of gout significantly differs between male and female

R. te Kampe[1], C. van Durme[1], M. Janssen[2], A. Boonen[1], T. Jansen[2]

[1]Maastricht University Medical Center, Maastricht, Netherlands, [2]VieCuri Medical Center, Venlo, Netherlands,

Objective

Gout, the most common type of inflammatory arthritis, is considered as a predominant male disease. Notwithstanding, there is an increased risk of gout in female after the menopause. Our objective was to assess differences in the clinical features between female and male patients.

Methods

Data of newly referred gout patients attending the rheumatology outpatient clinics of two hospitals in the Netherlands were used. We compared baseline characteristics of males and females regarding demographics, BMI, presence of tophi, medication use (diuretics, prophylaxis of gout and uric acid (UA) lowering drugs), serum and urine concentration of UA and creatinine, and comorbidities. Additional, fractional excretion of uric acid (FEUa) was compared. Independent t-tests and chi-square were used to assess differences statistically.

Results

66 female (16.6%) and 331 male (83.4%) patients with gout were included (table 1). At baseline, females compared to males had a significantly higher age, BMI and diuretic use. Females had also a significantly higher percentage of comorbidities, including hypertension, diabetes, and chronic kidney disease. There was no significant difference in serum UA concentration, current urate lowering and prophylactic medication, nephrolithiasis, presence of tophi and FEUa. Yet, the urine UA concentration was significantly lower in females.

Discussion

The clinical profile of gout in females significantly differs compared with males: significantly older, more advanced decrease in renal function, higher use of diuretics and higher prevalence of hypertension in the females. The start of diuretics has previously been associated with hyperuricemia and increases the risk of gout in the female population. Although diuretic use has proven to be a safe and effective first-line treatment for hypertension, the female gout population is enriched with diuretic use and a decreased renal function when compared with the male, and possibly diuretic use in the elderly hypertensive female needs reconsideration. Furthermore, despite the fact that the FEUa was similarly distributed, females did seem to have a lower urinary UA excretion. However, the number of patients with tophi and nephrolithiasis and the serum UA level is comparable between the sexes. This suggests that the urate burden is similar but that the clinical profile for the development of gout differs due to the UA production vs excretion.

Conclusion

In-depth analysis of this population underlines the differences in female and male gout patients, which highlight the need for more research into pathophysiology and management of gout between sexes.

Table 1: Baseline characteristics of the female and male patients separately.

Variable	Females	Males	P-value
Mean age, years (SD)	72.6 (11.7)	63.3 (12.9)	***<0.001***
BMI, kg/m^2 (SD)	30.1 (5.2)	28.7 (4.7)	***0.034***
Diuretic use (%)	63.6	27.8	***<0.001***
Hypertension (%)	78.8	60.1	***0.004***
Diabetes (%)	50.0	22.7	***<0.001***
CKD , eGFR (SD)	46.4 (24.2)	62.5 (22.9)	***<0.001***
Serum UA, mmol/L (SD)	0.51 (0.17)	0.48 (0.13)	0.262
Nephrolithiasis (%)	12.1	10.9	0.769
Tophi (%)	37.9	33.8	0.528
Urine UA, mmol/L (SD)	1.4 (1.1)	2.0 (1.5)	***0.029***
FEUa (%)	5.1 (3.0)	4.4 (1.7)	0.210

P_46

Efficacy of sarilumab in patients with rheumatoid arthritis with and without previous response to tocilizumab

P. Verschueren[1], P. Emery[2], H. Van Hoogstraten[3], Q. Dong[3], E. Mangan[4], A. Den Broeder[5]
[1]UZ Leuven, Leuven, Belgium, [2]Leeds Institute of Rheumatic & Musculoskeletal Medicine, Leeds, United Kingdom, [3]Sanofi Genzyme, Bridgewater, Nj,United States of America, [4]Regeneron Pharmaceuticals, Inc, Tarrytown, Ny,United States of America, [5]Rheumatology, Sint Maartenskliniek, Nijmegen ,

Background
Sarilumab is an IL-6R inhibitor recently approved for the treatment of rheumatoid arthritis (RA). To help clinical decision making, we studied the response rate on open-label sarilumab treatment in patients previously treated with tocilizumab, the other IL-6R inhibitor approved for RA. In the ASCERTAIN trial (NCT01768572), patients were randomized 1:1:2 to 24 weeks of sarilumab 150 mg sc every 2 weeks (q2w; n=49), sarilumab 200 mg sc q2w (n=51), or tocilizumab 4 mg/kg iv q4w (n=102) increased to 8 mg/kg at investigator's discretion if clinically indicated as per the US label; each added to conventional synthetic disease-modifying antirheumatic drug (csDMARD) background therapy. Patients who completed ASCERTAIN were eligible to enroll in an open-label extension study of sarilumab 200 mg sc q2w (EXTEND, NCT01146652), with csDMARDs as specified in the previous study.
Objectives
To examine outcomes for patients who switched from tocilizumab in ASCERTAIN to open-label sarilumab in EXTEND.
Methods
In this post hoc analysis, patients were recorded as responders or non-responders at the end of ASCERTAIN and at Weeks 12 and 24 of EXTEND according to each of: clinical disease activity index (CDAI) ≤2.8, CDAI ≤10.0, disease activity score (DAS)-28 CRP <2.6, DAS-28 CRP <3.2, and American College of Rheumatology (ACR)20/50/70 response criteria.
Results
A total of 168 patients entered EXTEND from ASCERTAIN, or whom 93 had been in the tocilizumab group (last tocilizumab dose 4 mg/kg in 37 patients and 8 mg/kg in 56 patients). After switch to sarilumab, response was achieved in an additional number of patients who were non-responders on tocilizumab at the end of ASCERTAIN (Table). The reverse, response loss in tocilizumab responders, was infrequent. Patients who switched from tocilizumab 4 mg/kg or 8 mg/kg achieved similar response rates.
Conclusions
These results may indicate that clinical improvements can be attained in a relevant proportion of tocilizumab non-responders with switch to sarilumab, irrespective of previous tocilizumab dose, and the majority of patients responding to tocilizumab maintain response when switching to sarilumab.
Acknowledgements
Study funding and medical writing support (Matt Lewis, Adelphi) provided by Sanofi and Regeneron Pharmaceuticals, Inc. Abstract previously presented at EULAR 2018.

Table 1

Last tocilizumab dose, mg/kg	Week in EXTEND	CDAI		DAS28-CRP				
		≤2.8	≤10	<2.6	<3.2	ACR20	ACR50	ACR70
		Non-responders at the end of ASCERTAIN with response in EXTEND (%)[a,b]						
4	12	3/27 (11)	7/18 (39)	8/23 (35)	8/18 (44)	3/5 (60)	8/19 (42)	7/25 (28)
	24	4/25 (16)	7/16 (44)	9/22 (41)	10/17 (59)	3/4 (75)	6/17 (35)	5/22 (23)
8	12	7/48 (15)	9/31 (29)	13/36 (36)	8/21 (38)	2/11 (18)	14/30 (47)	9/43 (21)
	24	10/46 (22)	13/29 (45)	16/35 (46)	7/20 (35)	6/10 (60)	13/28 (46)	13/41 (32)
		Responders at the end of ASCERTAIN with response in EXTEND (%)[a,b]						
4	12	8/9 (89)	15/18 (83)	11/11 (100)	16/16 (100)	28/31 (90)	16/17 (94)	10/11 (91)
	24	6/8 (75)	15/17 (88)	9/10 (90)	14/15 (93)	27/29 (93)	14/16 (88)	9/10 (90)
8	12	4/7 (57)	21/24 (88)	13/17 (76)	26/32 (81)	38/42 (90)	19/23 (83)	7/11 (64)
	24	5/7 (71)	20/24 (83)	14/18 (78)	28/33 (85)	39/43 (91)	19/24 (79)	9/12 (75)

[a]responder status according to measure listed in column heading; [b]subjects with missing measurements are excluded from numerator and denominator

P_47

Long term safety of filgotinib in the treatment of rheumatoid arthritis: week 108 data from a phase 2b open-label extension study

C.F. Allaart[1], R. Westhovens[2], A. Kavanaugh[3], L. Meuleners[4], C. Tasset[4], P. Harrison[4], A. van der Aa[4], R. Alten[5], T.W.J. Huizinga[1]

[1]Leiden University Medical Center, Leiden, Netherlands, [2]University Hospitals Leuven, Leuven, Belgium, [3]University of California San Diego, La Jolla,United States of America, [4]Galapagos NV, Mechelen,Belgium, [5]Schlosspark-Klinik, Berlin, Germany

Background

Filgotinib (FIL) is an orally administered, selective inhibitor of Janus Kinase 1 (JAK1) in Phase 3 development for the treatment of rheumatoid arthritis (RA).

Objectives

Assess the long term safety and efficacy of FIL in the DARWIN 3 open-label extension study.

Methods

Two 24-week Phase 2b studies were completed in patients (pts) with moderately to severely active RA (DARWIN 1, DARWIN 2; Ref 1, 2). Following study completion, pts were offered FIL in the ongoing DARWIN 3 extension study: 100 mg QD (US males), 200 mg QD or 100 mg BID. This report summarizes safety data from the first dose of FIL in the DARWIN program to 11 Oct 2017 and efficacy data from the DARWIN 3 baseline visit to Week 108, which all ongoing pts have completed.

Results

Of 877 pts, 790 (90%) completed DARWIN 1/2, and 739 (84%) enrolled in DARWIN 3; 603 (82%) were female, mean age 53 years. At analysis, 491/739 (66%) were on study. Cumulative patient years of exposure (PYE) was 1931, median time on study drug was 1072 days. Key data are summarized in Table 1. 87%, 68%, and 48% of pts achieved ACR20/50/70, respectively, and 72% achieved DAS28-CRP ≤3.2 (by observed case analysis).

Conclusion

Filgotinib long-term RA data demonstrate an acceptable safety and durable efficacy profile.

Table 1: Key Safety Events and Lab Abnormalities Per 100 PYE*

	Filgotinib + MTX		Filgotinib Monotherapy	Total* (N=739)
Events Per 100 PYE	100 mg BID (N=249)	200 mg QD (N=250)	200 mg QD (N=222)	
Treatment-emergent AEs (TEAEs)#	146.7	141.7	150.3	146.2
Serious TEAEs#	5.9	3.9	7.4	5.7
TEAEs for Infections	44.5	39.3	37.2	40.0
Serious TEAEs for Infections	1.2	0.6	2.2	1.3
Malignancy (excl. NMSC†)	0.8	0.4	0.7	0.6
Herpes Zoster	1.2	1.5	1.1	1.2
Deep Vein Thrombosis‡	0.2	0	0	0.1
Pulmonary Embolism‡	0.2	0	0	0.1
Active Tuberculosis	0	0	0	0
≥ Grade 3 Laboratory Abnormalities				
Hemoglobin ↓	0.5	0.1	0	0.2
Lymphocytes ↓	1.2	0.9	0.4	0.8
Neutrophils ↓	0.3	0.1	0.2	0.2
Platelets ↓	0	0.3	0	0.1
ALT ↑	0.2	0.1	0.2	0.2
Creatinine ↑	0.3	0	0	0.1
LDL ≥ 190 mg/dL	17.0	5.5	18.4	13.1
HDL <40 mg/dL	5.4	7.3	6.9	7.1

*Treatment groups with fewer than 10 subjects were omitted for clarity; †Non-melanoma skin cancer; ‡Single patient DVT leading to PE

P_48

Methods for the analysis of adherence data from a medication event monitoring system (MEMS): a systematic review

L. Hartman[1], W. Lems[1], M. Boers[2]

[1]VU medisch centrum, Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands, [2]Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, Netherlands

Background

Bottles with an electronic cap are regarded as the gold standard to measure medication adherence. The cap contains an electronic device which records the date and time of each opening and closing of the bottle. This is termed Medication Event Monitoring System (MEMS). To our knowledge, there is no standard method to summarize and analyze the data from MEMS.

Methods

A literature search was conducted in July 2017 in the databases PubMed, Embase and Cochrane. Search terms were related to the following Medical Subject Headings (MESH) search terms: medication (non)adherence/compliance, medication persistence, chronic disease/illness, chronically ill, medical electronics, treatment, (drug) therapy, data analysis, statistical study.

Results

We identified 1493 articles, and excluded 1127 off-topic articles and 48 double entries. In the end, 207 articles were included.

The mean age of the patients was 52 (standard deviation 46) years. A total of 62 different health conditions were studied. Most patients had human immunodeficiency virus (29%) or heart failure (10%). The MEMS cap was used for a median of 3 months (interquartile range: 4; range: 1 week-24 months).

Outcome measures

Most studies computed an adherence score, expressed as the percentage of days on which the correct dose of medication was taken. The threshold to mark people as adherent was most frequently (38 studies) set at 80% (range 67-95%). Timing compliance (i.e. the percentage of doses taken at the appropriate time) and dose compliance (i.e. the percentage of correct doses taken on each day) were calculated in 14% and 23% of the studies, respectively. In addition, 4% of the studies calculated ‘drug holidays’, i.e. periods of a certain number of days on which the medication bottle was not opened, followed by a bottle opening.

Statistical analyses

Multilevel modelling and slopes in combination with one-sample t-tests were used to examine adherence patterns over time.

Ten studies assessed an intervention to improve adherence. Generalized Estimating Equation (GEE) model (n=4), ANOVA, multilevel modeling, a summary analysis (details not reported), McNemar’s exact, t or Wilcoxon test were used to compare differences in adherence before and after an intervention.

Conclusions

Apart from the adherence score threshold, often set at 80%, we found that many different outcome measures and methods were used for the analysis of MEMS data, pointing to a lack of standardization. Apparently, there is no consensus on the best outcome measures and a lack of validation studies that compare different methods to analyze MEMS data.

P_49

Extra-articular manifestations are associated with poor quality of life and clinical outcome in patients with axial spondyloarthritis

R.G. van der Meer[1], S. Arends[1], S. Kruidhof[1], R. Bos[2], H. Bootsma[1], F. Wink[2], A. Spoorenberg[1]
[1]UMCG, Groningen, Netherlands, [2]Medisch Centrum Leeuwarden, Leeuwarden, Netherlands

Background
In the 1960s, the association between axial spondyloarthritis (SpA) and extra-articular manifestations (EAMs), acute anterior uveitis (AAU), inflammatory bowel disease (IBD) and psoriasis, was first reported. Still, knowledge of axial SpA disease outcome associated with the development of EAMs is scarce.
Objectives
To investigate the prevalence and 4-year incidence of EAMs and to explore associations of newly developed EAMs with disease outcome after 4 years of follow up in a large cohort of axial SpA patients.
Methods
All consecutive patients fulfilling the modified New York criteria for AS or the ASAS criteria for axial SpA from the prospective observational Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort with a baseline visit between November 2004 and December 2011 were included in the analyses. Baseline and follow-up data of EAMs from the GLAS database were verified in the medical records. EAMs were only recorded and used for analyses when a description of the diagnosis by an ophthalmologist, gastroenterologist or dermatologist was present. Prevalence and 4-year incidence of EAMs was calculated and comparative analyses regarding disease outcome was performed.
Results
421 axial SpA patients were included with a mean age of 43.4 ± 12.5 years, 65% were male, mean symptom duration was 17.4 ± 11.7 years, 78% were HLA-B27 positive, mean ASDAS was 3.3 ± 1.1 and 66% started TNF-α inhibitors at baseline. Of the 421 patients, 132 (31.4%) had a positive history of one or more EAMs: 104 (24.8%) AAU, 40 (9.5%) IBD, and 18 (4.3%) psoriasis. Of the 362 patients with 4-year follow-up data, 57 (15.7%) patients developed an EAM: 48 (13.3%) patients AAU, of which 13 (4.8%) had a first episode and 35 (9.8%) had recurrent AAU, 7 (1.9%) patients developed IBD, and 3 (0.8%) patients developed psoriasis.
Patients who developed a new EAM without a history of an EAM at baseline had higher ASQoL (mean 10.0 vs. 5.9, p=0.001), larger occiput to wall distance (median 6.3 vs. 2.0, p=0.021) and also the modified Schober test was more limited (mean 12.6 vs. 13.6, p=0.014) after 4 years of follow-up. The difference found for BASFI was not significantly significant (mean 4.4 vs. 3.4, p=0.12).
Conclusions
The prevalence rates of EAMs in our cohort are similar as found in other axial SpA studies. The 4-year incidence of EAMs was relatively low. However, these axial SpA patients showed worse quality of life and clinical outcome than patients without a newly developed EAM.

P_50

Female patients show a poorer treatment response and adherence to TNF treatment: a review

T. Rusman[1], R.F. van Vollenhoven[2], I.E. van der Horst-Bruinsma[2]
Amsterdam Rheumatology and immunology Center /VU University Medical Center, Amsterdam, Netherlands

Background

Some studies indicate a poorer treatment response on TNF inhibitor treatment in female axial spondyloarthritis patients [1-3]. Despite these indications, in many studies in axial spondyloarthritis the number of women included is low and the analyses are often not stratified for sex [4].

Objective

The purpose of the review was to aggregate the existing data on gender and sex differences in treatment response and adherence in axial spondyloarthritis , in order to increase the awareness of female axial spondyloarthritis patients, since there is still under recognition.

Method

A pubmed and google scholar search was performed using the search terms, individual and combined: ankylosing spondylitis, axial spondyloarhritis, gender or sex differences, women/woman, men/man, male/female, treatment response, treatment adherence, tumor necrosis factor, TNF inhibitor, switch. The abstracts of the identified articles were assessed for usability.

Results

After the identification process, twelve articles were identified which gave sufficient data on gender/sex differences in treatment response and adherence. Female patients show a significant lower level of TNF inhibitor treatment response (ASDAS: ankylosing spondylitis disease activity score and BASDAI: bath ankylosing spondylitis disease activity index) [2]. Furthermore, female patients showed a double risk at lower drug adherence compared to males [3]. In addition, significantly more female patients switched TNF inhibitor treatment, which indicate worse treatment adherence in females and may indicate a lower treatment response [1]. Some predictors were associated with a better treatment response, such as the presence of the HLA-B27 antigen, absence of enthesitis, short disease duration and being TNF inhibitor naive [1,5]. All these predictors were negatively associated with female axial spondyloarthritis patients.

Conclusion

In conclusion, treatment efficacy of TNF inhibitor is significantly lower in women compared to men with axial spondyloarthritis and they have a significantly lower drug adherence.

References

[1] Deodhar et al. Semin Arthritis Rheum. 2017;47(3):343-350
[2] van der Horst-Bruinsma et al. Ann Rheum Dis. 2013;72(7):1221-4;
[3] Glintborg et al. Ann Rheum Dis. 2010;69(11):2002-8;
[4] Tannenbaum C, et al. Pharmacol Res. 2017;121:83-93;
[5] Pavelka et al. Clin Exp Rheumatol. 2009;27(6):958-63

P_51

Frailty in elderly patients with rheumatoid arthritis; a cross-sectional study

M.G.B. van Onna[1], S. Oetsma[1], M. Starmans[2], R. Peeters[2], A. Boonen[1]

[1]Maastricht Universitair Medisch Centrum, Maastricht, Netherlands, [2]Zuyderland Medical Center, Heerlen, Netherlands,

Introduction

Frailty has been recognized as an important geriatric syndrome and is best described as 'a clinically recognizable state of increased vulnerability resulting from an age-associated decline in reserve and function in multiple physiological systems limiting the ability to cope with stressors, leading to adverse health outcomes'.(1) Although validated patient-reported measures to assess frailty are available, knowledge on frailty among patients with rheumatoid arthritis (RA) is scarce.

Objective

To assess (1) the prevalence of frailty in an elderly RA population, (2) which frailty domains (physical, physiological and social) are most affected and (3) whether frail patients differ from non-frail patients with regard to disease activity, physical functioning and number of comorbidities.

Methods

In this cross-sectional study, consecutive patients with RA and ≥ 65 years were recruited from two hospitals. Besides measurement of demographic variables and the Disease Activity Score (DAS28-ESR), patients filled out four self-reported questionnaires: the Groningen Frailty Indicator (GFI: score 0-15; ≥4 indicates frailty); the Geriatric-8 (G8: score 0-17; score ≤14 indicates frailty); the Health Assessment Questionnaire (HAQ); and the Rheumatic Disease Comorbidity Index (RDCI). T-tests, chi-square tests and Fisher's exact tests (as appropriate) were used to analyze differences between frail and non-frail patients.

Results

80 persons (mean age 74.6 years; 66% female) participated; 54% was frail on the GFI, 55% on the G8 (33% were frail on both the GFI and G8). Females ($p<0.01$), lower educated people (GFI: $p<0.05$; G8: $p=0.06$) and RA patients who lived alone ($p<0.02$) were more often frail. Age did not significantly differ between the frail and non-frail group.

With regard to the GFI, frail RA patients scored particularly high on the items of the psychosocial domain: 'emptiness', 'missing people', 'feeling abandoned' and 'anxious of depressive feelings' (all $p<0.01$). Scores on the frailty domains of the G8 are shown in Table 1. The DAS28-ESR, measured in 59 patients, was significantly higher in frail participants (GFI: 3.0 ± 1.2 vs. 2.4 ± 0.8, $p=0.04$; G8: 3.1 ± 1.2 vs. 2.3 ± 0.8, $p<0.01$). In addition, the HAQ was higher in frail participants (GFI: 1.2 ± 0.7 vs. 0.5 ± 0.4, $p<0.01$; G8: 1.2 ± 0.7 vs. 0.5 ± 0.5, $p<0.01$). Depression was the only comorbidity significantly more present in frail compared to non-frail patients (26% vs. 3% on GFI and G8 ($p<0.01$)).

Conclusion

Frailty is highly prevalent in this elderly RA population and is not necessarily related to age or presence of comorbidity.

Table 1. Number of patients with difficulties in each domain of the Geriatric-8 (G8).

	G8 Frail (n=44)	G8 Non-frail (n=36)	P value
Food intake			
Strong decrease in food intake % (n)	0 (0)	0 (0)	*0.03*
Moderate decrease in food intake % (n)	10 (22.7)	2 (5.6)	
No change in food intake *n* (%)	34 (77.3)	34 (94.4)	
Weight loss			
Weight loss more than 3 kg *n* (%)	6 (13.6)	0 (0)	*<0.01*
Don't know % (n)	0 (0)	0 (0)	
Weight loss between 1 to 3 kg *n* (%)	10 (22.7)	0 (0)	
No weight loss % (n)	28 (63.6)	36 (100)	
Mobility			
Bed or chair bound *n* (%)	0 (0)	0 (0)	0.25
Mobile inside house *n* (%)	4 (9.1)	1 (2.8)	
Goes outside independently *n* (%)	40 (90.9)	35 (97.2)	
Neuropsychological problems			
Severe dementia or depression *n* (%)	0 (0)	0 (0)	*<0.01*
Moderate dementia or depression *n* (%)	15 (34.1)	1 (2.8)	
No psychological problems *n* (%)	29 (65.9)	35 (97.2)	
Body mass index			
BMI <19 *n* (%)	2 (4.5)	0 (0)	*<0.01*
19 ≤ BMI <21 *n* (%)	5 (11.4)	0 (0)	
21 ≤ BMI <23 *n* (%)	11 (25.0)	2 (5.6)	
BMI ≥ 23 *n* (%)	26 (59.1)	34 (94.4)	
Drugs			
More than 3 types of medication *n* (%)	41 (93.2)	24 (66.7)	*<0.01*
3 types of medication or less *n* (%)	3 (6.8)	12 (33.3)	
Health status			
Less healthy *n* (%)	15 (34.1)	1 (2.8)	*<0.01*
Don't know *n* (%)	3 (6.8)	4 (11.1)	
Equally healthy *n* (%)	18 (40.9)	17 (47.2)	
Healthier *n* (%)	8 (18.2)	14 (38.9)	
Age			
Age >85 *n* (%)	2 (4.6)	0 (0)	*0.04*
Age 80-85 *n* (%)	13 (29.5)	4 (11.1)	
Age <80 *n* (%)	29 (65.9)	32 (88.9)	

P_52

Is a positive family history of spondyloarthritis relevant for diagnosing axial spondyloarthritis once HLA-B27 status is known? Data from the ASAS, DESIR and SPACE cohorts

M. van Lunteren[1], D. van der Heijde[1], A. Sepriano[1], R. Landewé[2], I.J. Berg[3], M. Dougados[4], L. Gossec[5], L. Jacobsson[6], R. Ramonda[7], M. Rudwaleit[8], J. Sieper[8], F.A. van Gaalen[1]

[1]Leiden University Medical Center, Leiden, Netherlands, [2]Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands, [3]Diakonhjemmet Hospital, Oslo,Norway, [4]Cochin Hospital, Paris Descartes University, Paris, France, [5]Sorbonne Université, UPMC Université Paris 06, GRC-08, Paris, France, [6]University of Gothenburg, Gothenburg, Sweden, [7]University of Padova, Padova, Italy, [8]Charité Campus Benjamin Franklin, Berlin, Germany

Background

A positive family history (PFH) of spondyloarthritis (SpA), in particular a PFH of ankylosing spondylitis (AS) or acute anterior uveitis (AAU), can be used to identify HLA-B27 carriership in chronic back pain patients[1]. It is unknown if a PFH contributes to diagnosing axSpA once HLA-B27 status is known.

Objective

To investigate in three independent axSpA cohorts if an ASAS PFH, a PFH of AS or a PFH of AAU contributes to a diagnosis of axSpA in patients with known HLA-B27 status.

Methods

Baseline data of patients suspected of axial SpA (axSpA) in the ASAS, DESIR and SPACE cohorts were analysed. In each cohort, univariable logistic regression models were performed with HLA-B27 status and ASAS PFH as determinants and a clinical axSpA diagnosis as outcome. The analyses were repeated in multivariable models with both determinants. The same analyses were performed for a PFH of AS or AAU.

Results

In total, 1,964 patients suspected of axSpA were analysed (ASAS n=594, DESIR n=647, SPACE n=577). Patients from the ASAS, DESIR, and SPACE cohorts, respectively 46%, 47%, and 38% were male; had a mean (SD) symptom duration of 85.7 (108.4), 18.2 (10.5), and 13.3 (7.1) months; 23%, 39%, and 38% had an ASAS PFH, 52%, 58%, and 43% were HLA-B27 positive, and 62%, 47%, and 54% were diagnosed with axSpA. In the univariable analysis, HLA-B27 status was significantly associated with an axSpA diagnosis in all three cohorts (see Table 1). An ASAS PFH and a PFH of AAU were univariately associated with an axSpA diagnosis in the SPACE cohort, but not in the ASAS and DESIR cohort. A PFH of AS was associated with diagnosis of axSpA in the ASAS cohort, but not in the DESIR and SPACE cohorts. In the multivariable models, HLA-B27 was independently and positively associated with a diagnosis of axSpA but such an independent positive association was not found for an ASAS PFH in any cohort (Table 1). Similarly, a PFH of AS did not have an independent positive association with an axSpA diagnosis in any cohort (Table 2). Similar results were found for PFH of AAU (ASAS cohort: HLA-B27 OR:6.9 (95%CI:4.7-10.1), ASAS PFH OR:0.4 (95%CI:0.08-1.8); DESIR cohort: HLA-B27 OR:2.1 (95%CI:1.5-2.9), ASAS PFH OR:1.1 (95%CI:0.5-2.3); SPACE cohort: HLA-B27 OR:10.7 (95%CI:7.0-16.3), ASAS PFH OR:0.8 (95%CI 0.3-1.8)).

Conclusions

When diagnosing axSpA, a PFH is no longer relevant once HLA-B27 status is known.

References

[1]Ez-Zaitouni et al (2017), AR&T 2017;19(1):118.

Table 1 Logistic regression analysis between ASAS PFH, HLA-B27, and clinical axSpA diagnosis in the ASAS, DESIR, and SPACE cohort

	axSpA+	axSpA-	OR (95%CI)	p-value
ASAS cohort				
Univariable analysis: HLA-B27				
HLA-B27+	**254**	**56**	**6.7 (4.7-9.8)**	**<0.001**
HLA-B27-	114	170	1.0 (ref)	(ref)
Univariable analysis: ASAS PFH				
ASAS PFH+	91	44	1.4 (0.9-2.0)	0.138
ASAS PFH-	277	182	1.0 (ref)	(ref)
Multivariable analysis: HLA-B27 and ASAS PFH				
HLA-B27+	**254**	**56**	**6.9 (4.7-10.2)**	**<0.001**
ASAS PFH+	91	44	0.9 (0.6-1.4)	0.561
DESIR cohort				
Univariable analysis: HLA-B27				
HLA-B27+	**204**	**172**	**2.1 (1.5-2.9)**	**<0.001**
HLA-B27-	98	172	1.0 (ref)	(ref)
Univariable analysis: ASAS PFH				
ASAS PFH+	117	132	1.0 (0.7-1.4)	0.900
ASAS PFH-	185	213	1.0 (ref)	(ref)
Multivariable analysis: HLA-B27 and ASAS PFH				
HLA-B27+	**204**	**172**	**2.1 (1.5-2.9)**	**<0.001**
ASAS PFH+	117	132	1.0 (0.7-1.3)	0.772
SPACE cohort				
Univariable analysis: HLA-B27				
HLA-B27+	**205**	**41**	**10.3 (6.9-15.5)**	**<0.001**
HLA-B27-	108	223	1.0 (ref)	(ref)
Univariable analysis: ASAS PFH				
ASAS PFH+	**132**	**86**	**1.5 (1.1-2.1)**	**0.018**
ASAS PFH-	181	178	1.0 (ref)	(ref)
Multivariable analysis: HLA-B27 and ASAS PFH				
HLA-B27+	**205**	**41**	**10.4 (6.9-15.7)**	**<0.001**
ASAS PFH+	132	86	1.0 (0.7-1.5)	0.921

Statistically significant associations are printed in bold. ASAS, Assessment of SpondyloArthritis international Society; (ax)SpA, (axial) spondyloarthritis; CI, confidence interval; HLA-B27, human leucocyte antigen B27; OR, odds ratio; PFH, positive family history.

Table 2 Logistic regression analysis between a PFH of AS, HLA-B27, and clinical axSpA diagnosis in the ASAS, DESIR, and SPACE cohort

	axSpA+	axSpA-	OR (95%CI)	p-value
ASAS cohort				
Univariable analysis: HLA-B27				
HLA-B27+	**254**	**56**	**6.7 (4.7-9.8)**	**<0.001**
HLA-B27-	114	170	1.0 (ref)	(ref)
Univariable analysis: PFH of AS				
PFH of AS+	**65**	**22**	**2.0 (1.2-3.3)**	**0.009**
PFH of AS-	303	204	1.0 (ref)	(ref)
Multivariable analysis: HLA-B27 and PFH of AS				
HLA-B27+	**254**	**56**	**6.9 (4.6-10.2)**	**<0.001**
PFH of AS+	65	22	0.9 (0.5-1.7)	0.800
DESIR cohort				
Univariable analysis: HLA-B27				
HLA-B27+	**204**	**172**	**2.1 (1.5-2.9)**	**<0.001**
HLA-B27-	98	172	1.0 (ref)	(ref)
Univariable analysis: PFH of AS				
PFH of AS+	63	64	1.2 (0.8-1.7)	0.461
PFH of AS-	239	281	1.0 (ref)	(ref)
Multivariable analysis: HLA-B27 and PFH of AS				
HLA-B27+	**204**	**172**	**2.1 (1.5-2.9)**	**<0.001**
PFH of AS+	63	64	1.0 (0.6-1.4)	0.829
SPACE cohort				
Univariable analysis: HLA-B27				
HLA-B27+	**205**	**41**	**10.3 (6.9-15.5)**	**<0.001**
HLA-B27-	108	223	1.0 (ref)	(ref)
Univariable analysis: PFH of AS				
PFH of AS+	63	41	1.4 (0.9-2.1)	0.153
PFH of AS-	250	223	1.0 (ref)	(ref)
Multivariable analysis: HLA-B27 and PFH of AS				
HLA-B27+	**205**	**41**	**13.4 (8.4-21.4)**	**<0.001**
PFH of AS+	**63**	**41**	**0.4 (0.2-0.8)**	**0.004**

Statistically significant associations are printed in bold. AS, Ankylosing Spondylitis; ASAS, Assessment of SpondyloArthritis international Society; (ax)SpA, (axial) spondyloarthritis; CI, confidence interval; HLA-B27, human leucocyte antigen B27; OR, odds ratio; PFH, positive family history.

P_53

Preferences of patients with rheumatoid arthritis regarding disease modifying anti-rheumatic drugs: a discrete choice experiment

M. van Heuckelum[1], E.G.E. Mathijssen[1], M. Vervloet[2], A.E.R.C.H Boonen[3], R. Hebing[4], A. Pasma[5], H.E. Vonkeman[6], M. Wenink[1], B.J.F. van den Bemt[1], L. van Dijk[2]

[1]Sint Maartenskliniek, Nijmegen, Netherlands, [2]Nivel, Utrecht, Netherlands, [3]MUMC+, Maastricht, Netherlands, [4]Reade, Amsterdam, Netherlands, [5]Erasmus MC, Rotterdam, [6]Medisch Spectrum Twente, Enschede, Netherlands

Background

Adherence to disease modifying anti-rheumatic drugs (DMARDs) in rheumatoid arthritis (RA) patients varies from 30-90%, which may be partly due to trade-offs patients make regarding treatment benefits and drawbacks[1]. Tailoring treatment options to these trade-offs might (implicitly) motivate patients to adhere to their drugs.

Objective

The aim of this study is to identify subgroups in rheumatoid arthritis patients based on their preferences towards DMARD characteristics, and to identify characteristics associated with subgroup membership.

Methods

A discrete choice experiment based on a literature review, expert recommendations and focus groups was used to elicit preferences. In this multicentre study, patients were asked to state their choice over two different hypothetical treatment options, described by seven DMARD characteristics and three levels within each characteristic (e.g. route of administration: oral, subcutaneous and intravenous). Inclusion criteria were: rheumatoid arthritis according to the ACR/EULAR2010 criteria, using at least one DMARD, and aged ≥18 years. Latent class analysis and multinomial logistic regression were used to identify subgroups and characteristics (beliefs about medicines, patient- and disease-related variables) associated with subgroup membership.

Results

Among 325 participating rheumatoid arthritis patients, three subgroups with the following segment sizes were identified: an administration-driven subgroup (45.6%), a benefit-driven subgroup (29.7%), and an indifferent subgroup (24.7%). In the administration-driven subgroup, the oral route of administration was strongly preferred over subcutaneous and intravenous administration. Current bDMARD use (RRR:0.50, 95%CI:0.28-0.89) was significantly associated with assignment to the administration-driven subgroup, and high educational level (RRR:11.4, 95%CI:0.97-133.6) with assignment to the benefit-driven subgroup (indifferent subgroup as base scenario). Patients' concern beliefs did not contribute significantly to subgroup membership, whereas a near significant association between patients' necessity beliefs and membership of the benefit-driven subgroup was found (RRR:1.12, 95%CI:1.00-1.23, P=0.055).

Conclusion

Three subgroups with different preferences were identified. Integrating these preferences in medication treatment decisions may improve adherence. Discriminating patients based on their beliefs about medicines, and patient and clinical characteristics is complex.

P_54

Switching from Adalimumab to Sarilumab is Associated with Comparable Efficacy but Lower Functional Improvement versus Continuous Sarilumab Monotherapy through 48-Week Open-label Extension (OLE) of the Phase 3 MONARCH Trial

G.R. Burmester[1], G. St John[2], M. Iglesias-Rodriguez[3], C.C. Hu[3], T. Raskina[4], H. Amital[5], A. Gomez-Centeno[6], A. Rubbert-Roth[7]

[1]Charité - University Medicine Berlin, Berlin, Germany, [2]Regeneron Pharmaceuticals, Inc, Tarrytown, Ny, United States of America, [3]Sanofi Genzyme, Bridgewater, Nj,United States of America, [4]Kemerov State Medical Academy of Roszdrav, Kemerovo, Russian Federation, [5]Sheba Medical Center, Tel-Hashomer, [6]Corporació Sanitària Parc Taulí, Barcelona, Spain, [7]Klinik fuer Rheumatologie, Kantonsspital St. Gallen, St. Gallen, Switzerland

Background

Sarilumab is a human mAb blocking IL-6Rα. In Phase 3 MONARCH (NCT02332590), sarilumab (200 mg subcutaneously [SC] every 2 wks [q2w] for 24 wks) was superior to adalimumab monotherapy (40 mg SC q2w) in reducing disease activity and improving physical function in RA patients (pts) with an inadequate response or intolerance to methotrexate.

Objectives

To assess whether pts who achieved clinical response on sarilumab during MONARCH sustained this response in the OLE and to evaluate efficacy and safety of switching from adalimumab to sarilumab vs continuous sarilumab treatment.

Methods

Pts completing the double-blind phase of MONARCH were eligible for the ongoing OLE, in which all pts receive sarilumab (200 mg SC q2w) for a maximum duration of 276 wks. Disease activity, physical function, and safety were assessed regularly.

Results

320/369 Pts enrolled in MONARCH entered the OLE; pts either switched from adalimumab to sarilumab (n=155) or continued on sarilumab (n=165). At OLE entry (Wk 24 of the double-blind phase), the mean Δ from baseline DAS28-ESR was –2.28 in the switch group vs -3.36 in the continuation group, and by Wk 48 was -4.06 vs -4.18, respectively. By Wk 48 of the OLE, the proportion of pts in the switch and continuation groups who achieved DAS28-ESR≤3.2 was 61.3% vs 61.2%, DAS28-ESR<2.6 was 43.9% vs 49.7%, and DAS28-CRP<2.6 was 52.9% vs 52.1%, respectively. From OLE entry to Wk 48, mean HAQ-DI improved in the switch group from 1.21 to 0.91, but did not reach the level of improvements in the continuation group (1.01 to 0.84). See table for ACR responses. After 166 vs 182 cumulative patient-years exposure in the switch vs continuation groups, treatment-emergent adverse events (TEAEs) were observed in 76.1% vs 70.9%, serious TEAEs in 11.0% vs 3.6%, and infections in 41.9% vs 35.8%, respectively, with 2 deaths in the switch group (malignancy; cerebrovascular accident) and 1 death (subarachnoid hemorrhage) in the continuation group. No GI related AEs (ulcerations, perforations or diverticulitis) were observed in either group.

Conclusions

Switching from adalimumab (40mg q2w) to sarilumab monotherapy (200 mg q2w) improved the signs and symptoms of RA to a similar level as continuous sarilumab treatment, and was associated with a lower HAQ-DI score, which may have resulted in numerical differences in ACR responses between the two groups.

Acknowledgements

Study funding and medical writing support (Vicki Cronin, Adelphi) provided by Sanofi and Regeneron Pharmaceuticals, Inc. Abstract previously presented at EULAR 2018.

Table 1

ACR responses & mean HAQ-DI in the OLE of MONARCH (OLE ITT Popn)				
	Wk 0 OLE		Wk 48 OLE	
	Switch group: Adalimumab 40 mg q2w → Sarilumab 200 mg q2w (N=155)	Continuation group: Sarilumab 200 mg q2w (N=165)	Switch group: Adalimumab 40 mg q2w → Sarilumab 200 mg q2w (N=155)	Continuation group: Sarilumab 200 mg q2w (N=165)
ACR20/50/70, % responders	68.4/35.5/14.2	79.4/50.9/26.1	77.4/59.4/38.1	81.2/63.0/41.8
HAQ-DI, mean	1.21	1.01	0.91	0.84

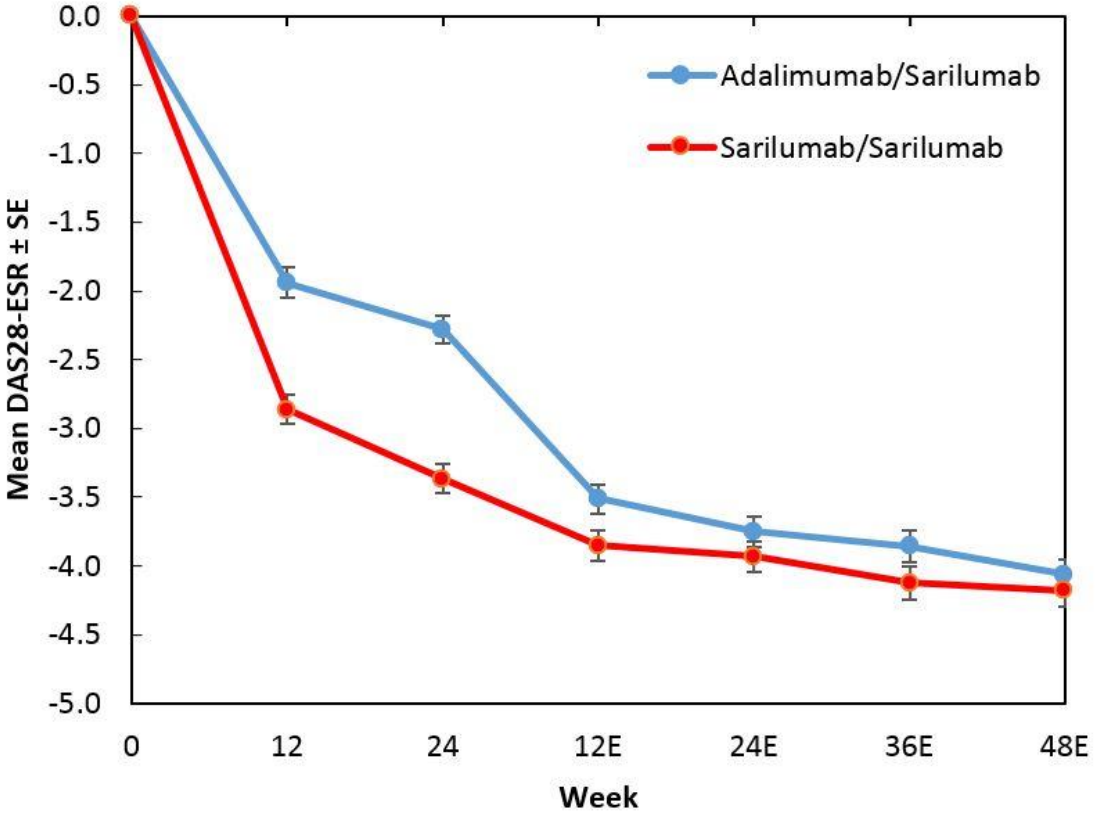


Figure: Mean Δ from baseline in DAS28-ESR (OLE population; as observed).

P_55

Remarkable international variability in reasons for non-participation in the GLORIA trial

L. Hartman[1], R. Bos[2], F. Buttgereit[3], M. Güler-Yüksel[4], R. Ionescu[5], M. Kok[4], W. Lems[1], M. Micaelo[6], D. Opris-Belinski[5], A. Pusztai[7], E. Santos[8], J. Da Silva[8], Z. Szekanecz[7], K. Zeiner[3], D. Zhang[2], M. Boers[9]

[1]VU medisch centrum, Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands, [2]Medisch Centrum Leeuwarden, Leeuwarden, Netherlands, [3]Charité, Berlin, Germany, [4]Maasstad Ziekenhuis, Rotterdam, Netherlands, [5]"Sf. Maria" Hospital, University of Medicine and Pharmacy "Carol Davila", Bucharest, [6]Instituto Português de Reumatologia, Lisbon, Portugal, [7]University of Debrecen, Faculty of Medicine, Debrecen, Hungary, [8]Reumatologia, Faculdade de Medicina e Hospitais da Universidade de Coimbra, Coimbra, Portugal, [9]Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, Netherlands,

Background

GLORIA is an ongoing large pragmatic trial that examines harm, benefit and costs of low-dose glucocorticoids added to the standard treatment of RA patients of 65 years or older. The eligibility criteria are non-restrictive: RA, age ≥65 years, disease activity score (DAS28) of ≥2.6, and no current glucocorticoid treatment. Patients with comorbidity are expressly included, and the impact of trial procedures on normal care is minimal. Nevertheless, inclusion proves to be challenging. We have prospectively sampled all the reasons for ineligibility across a number of centers in different countries participating in the GLORIA trial.

Methods

Rheumatologists from 8 centers in Germany, Hungary, The Netherlands, Portugal and Romania screened the patient list of at least two full clinic days. For each patient, the eligibility and all possible reasons of exclusion were recorded.

Results

In total, 385 patients were screened. Of these patients, 15 (4%) were eligible to participate in the GLORIA trial. In Germany, Romania and Portugal (Lisbon) none of the screened patients proved eligible.

The most common reasons for ineligibility were inactive disease and age (both 58%) (Table 1). Current glucocorticoid use was reported in 28%, 5% had a temporary reason (i.e. recent switch of therapy or glucocorticoid use), and 51% had more than one reason for ineligibility. We found remarkable differences between the sites in the distribution of the main reasons for ineligibility (Table 1).

Of the eligible patients, 1 was already participating, 3 were included after this screening, and 2 were currently considering participation; 9 declined participation (most common reasons: fear of glucocorticoids, not interested to participate, preference for GC injections or declining additional therapy).

Conclusions

In this prospective study, we found remarkable differences between countries in reasons for non-participation in our ongoing GLORIA trial. The willingness of eligible patients to participate was low in this elderly population, despite the pragmatic design. Earlier studies also showed that it is challenging to include elderly patients in a clinical trial (1, 2). Pre-screening of patients in potential sites can provide important information on the potential to recruit patients in a trial, but the actual willingness of patients to participate remains hard to predict.

Table 1: Percentages of patients ineligible for the GLORIA trial, per reason (patients can have more reasons)

Center	Age (%)	Disease activity (%)	Current glucocorticoid use (%)	Temporary reason (%)	Other reasons (%)
Total (n=370)	58	58	28	5	11
The Netherlands, Amsterdam (n=156)	54	70	22	5	11
The Netherlands, Rotterdam (n=43)	63	58	12	2	9
The Netherlands, Leeuwarden (n=46)	51	70	11	4	19
Germany, Berlin (n=23)	52	52	65	0	17
Portugal, Coimbra (n=21)	58	21	8	4	17
Portugal, Lisbon (n=10)	60	60	80	80	10
Hungary, Debrecen (n=46)	75	43	55	0	2
Romania, Bucharest (n=18)	56	22	44	0	6

P_56

Similar efficacy and safety of sarilumab 150 mg or 200 mg q2w regardless of primary or secondary failure with TNF inhibitors

R. Fleischmann[1], A. Spindler[2], A. Kivitz[3], D. Ching[4], E. Mangan[5], T. Kimura[5], M. Iglesias-Rodriguez[6], G. Burmester[7]
[1]Metroplex Clinical Research Center, Dallas, Tx, United States of America, [2]Universidad Nacional de Tucumán, TucumáN, Argentina, [3]Altoona Center for Clinical Research, Duncansville, Pa,United States of America, [4]Timaru Medical Specialists Ltd, Timaru,New Zealand, [5]Regeneron Pharmaceuticals, Inc, Tarrytown, Ny, [6]Sanofi Genzyme, Bridgewater, Nj, United States of America, [7]Free University and Humboldt University Berlin, Berlin, Germany

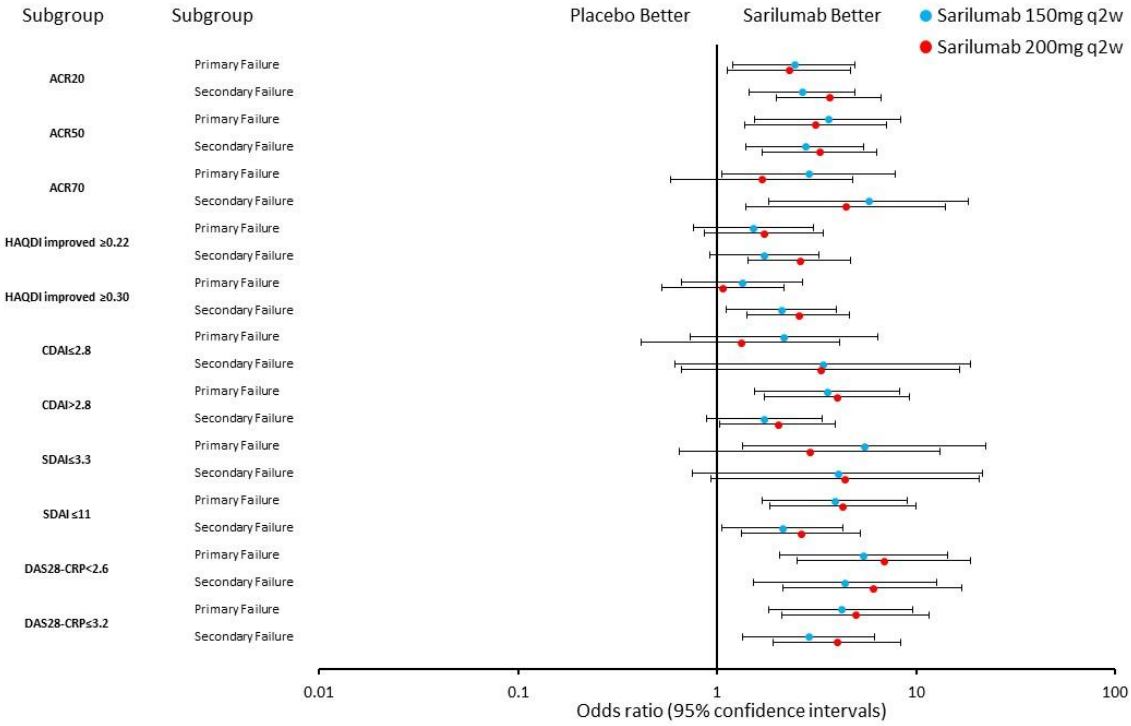
Background
Sarilumab (150 or 200 mg subcutaneously [SC] every 2 wks [q2w]) + csDMARDs demonstrated efficacy in adults with moderate-to-severely active rheumatoid arthritis (RA) with intolerance or inadequate response to prior TNFi treatment in TARGET (NCT01709578). Patients with an initial refractory response (primary [1°] failure) to TNFi may respond differently to subsequent treatment vs those who initially respond but lose TNFi effectiveness (secondary [2°] failure).
Objectives
This post hoc analysis examined efficacy and safety of sarilumab + csDMARDS in patients who had previously demonstrated 1° vs 2° TNFi failure.
Methods
TNFi failure (1° vs 2°) was investigator-determined on enrolment to TARGET. Patients who experienced 1° or 2° failure were randomized to placebo (n=75 and n=99), sarilumab 150 mg (n=72; n=91), or sarilumab 200 mg q2w (n=64; n=103), respectively. Disease activity, physical function (HAQ-DI), and safety were assessed at Wk 24.
Results
By Wk 24, ACR20/50/70 response rates and improvements in LS mean HAQ-DI were similar in both sarilumab dose groups and superior to placebo, irrespective of 1° vs 2° TNFi failure (Table). Odds ratios for the benefit of sarilumab over placebo according to ACR response rates, HAQ-DI, DAS28-CRP, CDAI and SDAI (Figure) showed no differences between patients with 1° vs 2° failures. No significant treatment by subgroup (1° vs 2° failure) interactions were observed. In the 1° failure group, treatment emergent adverse events (TEAEs; Table) occurred in 59.7%, 65.6% vs 45.3% (sarilumab 150, 200 mg vs placebo, respectively) of patients; and in 73.6% and 63.1% vs 52.5% with sarilumab 150, 200 mg vs placebo, respectively, in the 2° failure group. There was only one TEAE leading to death (placebo group) and one case each of venous thrombosis (200 mg sarilumab q2w, 2°) and pulmonary embolism (150 mg sarilumab q2w, 2°).
Conclusions
Key efficacy and safety measures were similar in patients treated with sarilumab + csDMARDs, regardless of previous 1° or 2° failure with TNFis.
Acknowledgements
Study funding and medical writing support (Vicki Cronin, Adelphi) provided by Sanofi and Regeneron Pharmaceuticals, Inc. Abstract previously presented at EULAR 2018.

Table 1

Table: Efficacy responses and percentage of patients experiencing AEs (≥5% in any subgroup) at Wk 24

	Primary failure			Secondary failure		
	Placebo (n=75)	**Sarilumab 150 mg q2w (n=72)**	**Sarilumab 200 mg q2w (n=64)**	**Placebo (n=99)**	**Sarilumab 150 mg q2w (n=91)**	**Sarilumab 200 mg q2w (n=103)**
Efficacy parameters						
ACR20/50/70, % Responders	33.3/18.7/12.0	51.4/37.5/23.6	51.6/37.5/15.6	35.4/18.2/4.0	59.3/39.6/19.8	66.0/41.7/15.5
CDAI, LS mean Δ from baseline (SE)	-15.28 (1.9)	-23.73 (1.9)	-22.73 (2.0)	-17.89 (1.6)	-24.42 (1.6)	-27.43 (1.5)
TEAEs (%)						
Neutropenia	1.3	12.5	10.9	0.0	13.2	12.6
UTI	6.7	1.4	7.8	7.1	5.5	6.8
Increased ALT	1.3	5.6	7.8	0.0	1.1	3.9
uRTI	5.3	1.4	4.7	2.0	3.3	2.9
Hypertriglyceridemia	1.3	8.3	6.3	2.0	3.3	1.0
Accidental overdose	4.0	1.4	6.3	2.0	6.6	2.9
Hypertension	0.0	0.0	6.3	4.0	1.1	2.9
Hypercholesterolemia	0.0	5.6	4.7	0.0	2.2	1.0
Diarrhea	5.3	0.0	4.7	2.0	1.1	1.9
RA	4.0	0.0	0.0	5.1	3.3	2.9
Injection site erythema	0.0	4.2	4.7	0.0	7.7	1.9
Nasopharyngitis	4.0	4.2	1.6	5.1	7.7	4.9

Figure 1


Subgroup
Subgroup
Placebo Better
Sarilumab Better
Sarilumab 150mg q2w
Sarilumab 200mg q2w
ACR20
ACR50
ACR70
HAQDI improved ≥0.22
HAQDI improved ≥0.30
CDAI≤2.8
CDAI>2.8
SDAI≤3.3
SDAI ≤11
DAS28-CRP<2.6
DAS28-CRP≤3.2
Primary Failure
Secondary Failure
0.01
0.1
1
10
100
Odds ratio (95% confidence intervals)

P_57

Efficacious transition from reference product infliximab to the biosimilar in daily practice

Z. Layegh[1], J. Ruwaard[2], R. c.f Hebing[3], M. j L`Ami[2], W. Van der Weele[2], M. t Nurmohamed[2], G. Wolbink[2], C. Krieckaert[2]
[1]1Amsterdam Rheumatology and immunology Center | Reade, Amsterdam, Netherlands, [2]Rheumatology and immunology Center | Reade, Amsterdam, Netherlands, [3]Reade, Rheumatology, Pharmacy. Amsterdam, The Netherlands

Background

The biosimilar of infliximab, approved in September 2013 for the treatment of rheumatic diseases. The biosimilar is non-inferior to the reference product of infliximab based on safety, quality and efficacy(1). In order to enable health care cost saving and efficient treatment, a transition to the biosimilar was deemed necessary.

Objectives

To evaluate the transition from the reference product to the biosimilar in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA).

Methods

Consecutive patients treated with reference product were switched to the biosimilar in the period July 2015 to June 2016 at the Amsterdam Rheumatology and immunology Center, Reade. Patients were informed by a letter about the transition to the biosimilar and were subsequently contacted by a nurse or the pharmacist for additional questions and whether they agreed upon the switch. Patients were advised to contact their treating rheumatologist when in doubt. Once agreed, the biosimilar was administered at the same dosage and interval as previous treatment with the reference product. Patients were followed until January 2018. The primary outcome was to evaluate the transition from the reference product to the biosimilar, secondary outcome was the change in disease activity measured with the Disease Activity Score in 28 joints using erythrocyte sedimentation rate (DAS28-ESR). Last available DAS28-ESR before switching and first available DAS28-ESR approximately 12 months after switching was used. In addition, the reason for discontinuation with infliximab or the restart with the reference product was recorded.

Results

In total 45 patients switched from the reference product to the biosimilar, 2 patients disagreed upon the switch and continued the reference product. The median treatment duration with infliximab in patients with RA and PsA was 11 (IQR 6-15) years (Table 1). During the follow-up period, 3 patients (7%) restarted the reference product due to subjective reasons, increase in disease activity was not objectified by the rheumatologist. The biosimilar was continued by 42 patients (93%). Furthermore, 2 patients switched to another biological due to lack of effect and in 1 biological therapy was stopped because of lung malignancy. The DAS28-ESR remained comparable before and after the switch, with a mean (SD) of respectively 2.34 (±1.02) and 2.31 (±1.11).

Conclusions

In our population, 93 % of the patients continued the biosimilar during the follow up period of two years. Three patients restarted the reference product, whilst retaining stable DAS28-ESR.

Table 1. Baseline demographics and disease characteristics of the 45 patients who switched from the reference product to biosimilar.

	RA (N=41)	PsA(N=4)	Total (N=45)
Demographic features			
Age, mean (SD) years	66 (15)	62 (6)	65 (14)
Female no. (%)	32 (78)	0 (0)	32 (71)
Male no. (%)	9 (22)	4 (100)	13 (29)
Disease duration, median (IQR) years	17 (12-23)	8 (6-12)	17 (11-23)
Disease-specific characteristics			
DAS28-ESR, mean (SD)	2.4(1.03)	1.6(0.61)	2.3(1.02)
Treatment-specific characteristics			
Duration infliximab use, median (IQR) years	11 (6-15)	5.5(5-9)	11 (6-15)
DMARD treatment			
Methotrexate no.(%)	27 (66)	4 (100)	31 (69)

RA = Rheumatoid arthritis; PsA = psoriatic arthritis DAS28-ESR = Disease activity score in 28 joints using erythrocyte sedimentation rate; conventional synthetic disease-modifying anti-rheumatic drugs.

P_58

Course and predictors of upper leg muscle strength over 4 years in subjects with knee osteoarthritis: data from the Osteoarthritis Initiative

A.H. de Zwart
Reade, Amsterdam, Netherlands

Background
In patients with knee osteoarthritis (OA) muscle weakness is strongly related to more pain and activity limitations, and is a risk factor for radiographic progression. Despite its important role, knowledge on the course and predictors of muscle strength over time is scarce.
Objectives
The aim of the present study is (i) to describe the course and (ii) to identify baseline predictors for upper leg muscle strength over time in subjects with knee OA.
Methods
Data were obtained from the progression cohort of the Osteoarthritis Initiative (OAI) database. The progression cohort includes subjects with frequent knee symptoms and radiographic tibiofemoral knee OA at baseline. Upper leg muscle strength was measured at baseline, 24 months and 48 months. Upper leg muscle strength of the index knee was expressed as the sum of both flexion and extension strength corrected for bodyweight (N/kg bodyweight). Potential baseline predictors included demographic, health and lifestyle related and OA-specific factors. Linear mixed model analyses were performed.
Results
A total of 1390 subjects with knee osteoarthritis were included. A statistically significant decrease in muscle strength over time was found (b = -.148, p < 0.01). On average subjects lost 5.2% of muscle strength over 48 months. Demographic predictors for lower muscle strength over time were older age, being female, higher BMI, being non-Caucasian. Health and lifestyle related predictors were lower protein intake (g/kg bodyweight), higher energy intake, and lower alcohol consumption. OA specific predictors were valgus and normal alignment of the knee, higher score on the WOMAC pain subscale, lower level of physical activity and use of pain medication at baseline.
Conclusions
Muscle strength declined over time in subjects with knee OA. Demographic, health and lifestyle related, and OA-specific predictors of the decrease of muscle strength were found. These predictors may help clinicians to identify and treat those patients at risk for a decline in muscle strength over time.

P_59

Assessing need and knowledge of advanced medical imaging in rheumatology

M.M. Cabri
VUMC, Amsterdam, Netherlands

Background

While there is a growing clinical need for application of advanced imaging techniques (e.g. MRI, ultrasound, CT, PET) as objective tools for both diagnostics and follow up of a broad spectrum of diseases there is an hiatus in knowledge to request and interpret these advanced imaging techniques by rheumatologists required for optimal clinical care[3-5] .

Objective

To create overview of the current communication methods between rheumatologists and radiologists regarding MRI and rheumatologists perspectives on the efficiency and effectiveness of the imaging requests and radiologists reports. Also to make an inventory of current knowledge and interpretation skills of rheumatologists concerning MRI.

Methods

A questionnaire is developed and with the collaboration of the Dutch Rheumatology Association (NVR) we are able to reach over 230 rheumatologists in the Netherlands with this questionnaire. This questionnaire is divided in 6 chapters (1. Population characteristics 2. Current communication 3. Skills in MR imaging 4. Wishes for communication from rheumatology group 5. Subjects for education and 6. Communication specifically with radiologists). This questionnaire will be distributed in the first week of May. Results are expected in the following two weeks.

Results

Our pilot assessment among rheumatologists at the annual Dutch rheumatology congress last year revealed that most rheumatologists have insufficient knowledge of MR imaging but also see a clear clinical need to learn more about interpretation of MRI and its clinical applications to address questions in clinical practice of rheumatology. This was confirmed by the trainers in rheumatology and the Dutch Rheumatology association. We have the same feedback from our “hands-on MRI rheumatology” course we developed in 2015.

In our pilot study we also determined that e-learning is the preferred method of learning for rheumatologists. The results from the extended questionnaire are to be expected before June 1st.

Conclusion

With the increasing clinical need to establish early diagnosis and development of precision medicine to increase treatment efficacy and to reduce costs, imaging will be increasingly applied in clinical care. Adequate basic knowledge of the non-radiologist medical specialists will contribute to proper selection and interpretation of imaging technique to optimize clinical care. This study reveals the clinical wishes from rheumatologists for advanced imaging communication with the imaging specialists.

P_60

Bright light therapy in rheumatoid arthritis to improve symptoms of fatigue and other disease outcomes: a randomized controlled pilot trial

G.E.A. Habers[1], C.F. Allaart[2], D.S. Veldhuijzen[1], A.H.M. van der Helm[2], E. Vreugdenhil[3], T.W.J. Huizinga[2], A.W.M. Evers[1]

[1]Health, Medical and Neuropsychology Unit, Faculty of Social Sciences, Leiden Uni, Leiden, Netherlands, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [3]Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, Netherlands

Background

A disturbed circadian rhythm has been found in patients with rheumatoid arthritis and may be an important underlying mechanism for frequently observed symptoms which reduce quality of life negatively (e.g. fatigue).

Objective

In the current study, the efficacy of a four-week bright light therapy program is examined for the first time in patients with rheumatoid arthritis. The primary objective is to explore the difference between an intervention group (active therapy) and a control group (sham therapy) in fatigue while taking into account baseline fatigue. As secondary objectives we explore 1) secondary efficacy outcomes (see Methods), 2) the potential of the therapy in delaying the circadian entrainment, 3) the four-week follow-up effects, and 4) (barriers to) therapy adherence, therapy acceptability as well as study feasibility and acceptability.

Methods

This study is a randomized, double blind, parallel-arm, placebo controlled pilot study that could serve as preparation for a future larger full-scale randomized controlled trial. Forty-eight adult patients with rheumatoid arthritis from the Department of Rheumatology of the Leiden University Medical Center will be recruited for this study. Eligible patients have elevated feelings of fatigue (Checklist Individual Strength subscale Fatigue≥27) and low disease activity or are in remission. In both therapy arms, light therapy glasses are worn in the home of the participant every day for 30 minutes in the evening (between 20-21h) during four consecutive weeks. The arms differ in the wavelength of light that is emitted. The primary outcome is assessed by the Checklist Individual Strength subscale Fatigue. Secondary outcomes are: pain and morning joint stiffness (Impact of Rheumatic diseases on General health and Lifestyle; subscale Pain), sleep (diary and Insomnia Severity Index), emotional well-being and general health status (RAND-36), depression (Hospital Anxiety and Depression Scale), and disease activity (Disease Activity Score). Circadian entrainment is assessed by the melatonin onset in saliva (as tested with Dim Light Melatonin Onset test) and a sleep diary.

Results

Data collection started January ‘18 and is expected to be finished in the summer of ‘18. We will discuss the background of the study, the used methods, and preliminary results.

Conclusion

This study evaluates in rheumatoid arthritis preliminary efficacy, feasibility, and acceptability of bright light therapy, which directs at the disturbed circadian rhythmicity observed in this population.

P_61

Training immune function through pharmacotherapeutic conditioning in juvenile idiopathic arthritis

R.M. Smits[1], D.S. Veldhuijzen[1], N.M. Wulffraat[2], A.W.M. Evers[1]

[1]Universiteit Leiden, Instituut Psychologie, Leiden, Netherlands, [2]Universitair Medisch Centrum Utrecht, Utrecht, Netherlands,

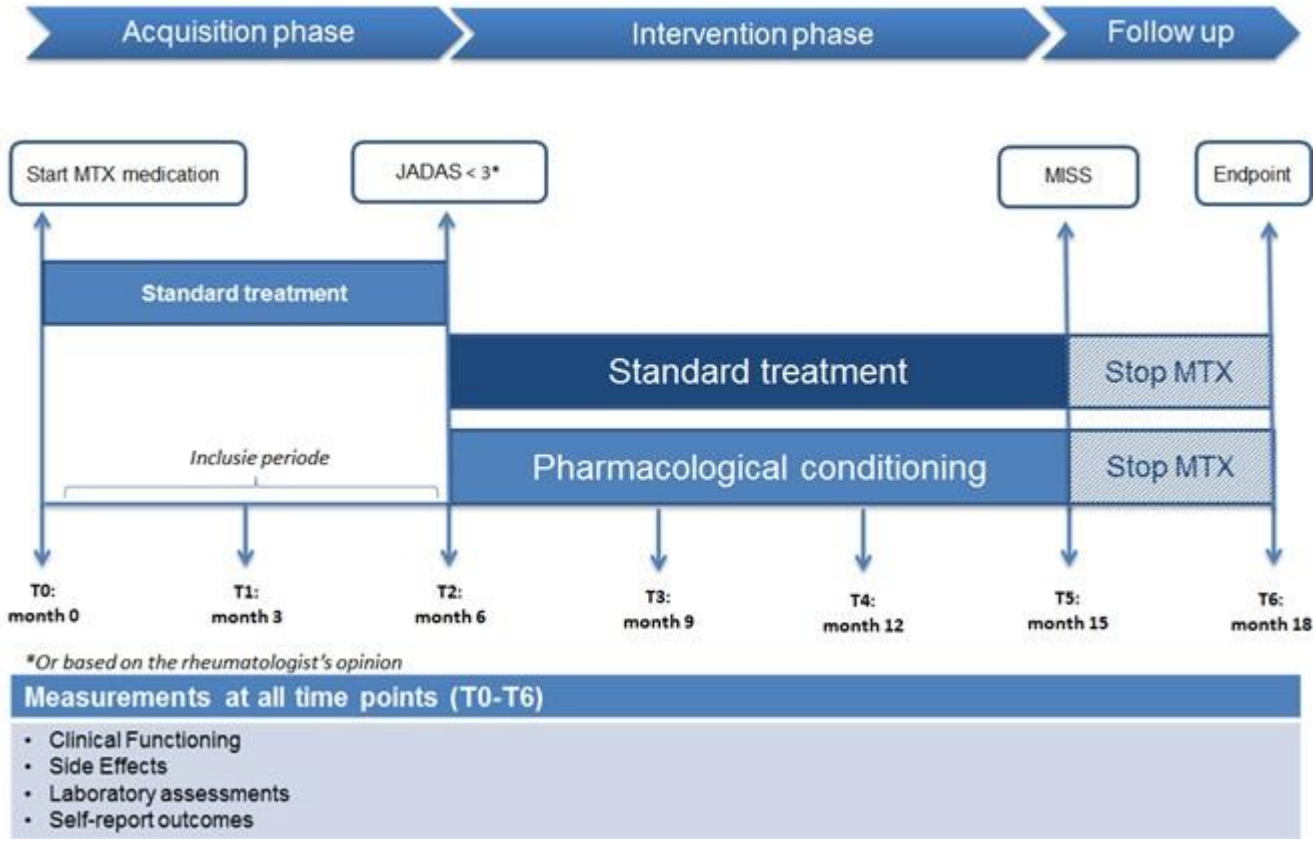
Background: Pharmacotherapeutic conditioning is a novel treatment approach where learning mechanisms and expectations (also known as placebo effects) are combined with drug therapy in order to obtain optimal treatment outcomes. By making use of these principles, it is possible to train immune functions combined with lower dosing of medication, such as with the anti-inflammatory drug methotrexate (MTX). Studies have showed that MTX intolerance is a well-known problem in the treatment for children with Juvenile Idiopathic Arthritis (JIA) with nearly half of the patients suffering from intolerance (Bulatovic, 2011). This study aims to reduce side effects by lowering intake of MTX through the application of pharmacotherapeutic conditioning in patients with JIA.

Methods: A double-blind randomized controlled trial will be conducted in academic medical centers in the Netherlands. Patients who are administered MTX for the first time are applicable to participate. Patients will receive standardized MTX dose for six months (12,5 – 15 mg/m² per week). After establishing a good response to MTX as assessed by low disease activity, patients will be randomized to the experimental period in one of two groups; 9 months of MTX treatment though a variable reinforcement design or a control group in which patients will continue on MTX standard dosing. Based on pharmacotherapeutic conditioning principles it is expected that treatment effects through variable reinforcement are optimized and side effects will be lower (as a result of lower MTX dosing in the conditioning group). In this case, treatment effects of methotrexate are less hampered by its accompanied side effects.

Findings: Data collection will start in 2018 and is expected to be completed 2021.

Discussion: Beneficial results from pharmacotherapeutic conditioning have been established in various clinical populations, such as psoriasis, irritable bowel syndrom, attention deficit hyperactivity disorder and more. However, it has not yet been studied in (chronic) inflammatory diseases. Previous studies have demonstrated the learning abilities of the immune system, and we now assess the potential application for children with JIA.

Figure 1: Design overview



.