Acknowledgement: Yutaro Yamada

Disclosure of Interests: Yutaro Yamada Speakers bureau: Abbvie, Chugai, Mitsubishi Tanabe, Masahiro Tada Speakers bureau: Abbvie, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical, Pfizer Japan, Takeda Pharmaceutical, Koji Mandai: None declared, Noriaki Hidaka: None declared, Kentaro Inui Speakers bureau: Takeda Pharmaceutical, Pfizer Japan, Daiichi-Sankyo Co.Ltd., Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co.Ltd., Eli-Lilly, Nippon Kayaku Co., Ltd., Maruho Co.,Ltd, Kaken Pharmaceutical Co.,Ltd., Hiroaki Nakamura: None declared

DOI: 10.1136/annrheumdis-2019-eular.1430

FRI0073

SWELLING OR TENDERNESS, WHICH ONE CORRESPONDS BETTER WITH ULTRASOUND-DETECTED SYNOVITIS?

Xiaoying Sun, Xuerong Deng, Wenhui Xie, Yu Wang, Zhuoli Zhang. Peking University First Hospital, Beijing, China

Background: Ultrasound (US) is a sensitive method for detecting joint inflammation in patients with rheumatoid arthritis (RA). The relationship between tender or swollen joints and ultrasound-detected synovitis has not been well explored in patients with RA.

Objectives: The purpose of the present study was to compare the correlation between ultrasound-detected synovitis and joint tenderness or swelling at the wrists and hands in RA patients.

Methods: Twenty-two joints, including bilateral wrists, proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, were respectively evaluated by physical examination (PE) and ultrasound scan in 258 RA patients. All patients had at least 1 tender or swollen joint out of 22 joints. Synovitis was detected by using semi-quantitative scoring systems (0-3) for grey scale(GS) and power Doppler(PD). Positive synovitis was defined as $GS \geq 2$ and/or $PD \geq 1$. All correlations among US variables and clinical variables were assessed using Spearman's rank correlation test. Cohen's kappa (κ) between clinical and sonographic findings was calculated.

Results: Their median age was 51.2 years, median disease duration was 57 months, with 83.33% females. The mean (SD) Disease Activity Score based on 28 joints (DAS28)-ESR and DS28-CRP were 4.47 ± 1.62 and 3.99 ± 1.51 , respectively. In a total of 5676 joints assessed, 968 swollen joints (17.05%) and 1296 tender joints (22.83%) were found, while on ultrasonography GS synovial hyperplasia was present in 801 (14.11%) joints, positive PD in 476 (8.38%) joints. There were more tender joints without swelling ($n=574$) than those swollen joints without tenderness ($n=246$). In all joints, higher κ coefficient was observed in joint swelling ($\kappa=0.367$, $p<0.01$) with ultrasound-detected synovitis compared with tenderness ($\kappa=0.281$, $p<0.01$). Similarly, swollen joint counts of 22 joints showed higher Spearman's correlation coefficient with either total GS scores ($r=0.499$, $p<0.01$) or total PD scores of 22 joints ($r=0.430$, $p<0.01$) than tender joint counts of 22 joints ($r=0.354/0.308$, $p<0.01$). GS and PD synovitis were more frequently detected in swollen joints without tenderness compared with tender joints without swelling. This discrepancy tend to be more significant in MCP2, MCP3, and MCP4 joints ($p<0.05$).

Conclusion: In RA patients with at least 1 tender or swollen joint of wrists and hands, a higher frequency of joint tenderness was observed than swelling. However, swelling had better agreement with ultrasound detected synovitis compared with tenderness. Joint swelling is more associated with ultrasound-detected synovitis than tenderness. Without swelling, joint tenderness tends to be less associated with ultrasound-detected synovitis.

REFERENCE:

- [1] Tan YK, Moorakonda RB, Allen JC Jr, Chew LC, Thumboo J. Back to the basics: Understanding joint swelling and tenderness at the wrist in rheumatoid arthritis through the use of ultrasonography. *Int J Rheum Dis*. 2018 Oct 21.

Acknowledgement: The authors thank all the colleagues in our department for kind cooperation in this project and the patients for participating in this study.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3601

Rheumatoid arthritis – biological DMARDs

FRI0074

UPDATE FOR THE CLINICAL PRACTICE: INTEGRATED, EVIDENCE-BASED APPROACH FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS

Mohammed Hassan Abu-Zaid¹, Yasser El Miedany², Mohammed A Mortada³, Waleed Hassan⁴, Mervat Eissa⁵, Yossra Atef⁶, Samah Ismail Nasef⁷, Hala Lotty⁸, Yomna Farag⁹, Ghada El Deriny⁹, Nadia El Arousy¹⁰, Maha El Gaafary¹¹, Dalia Mekawy¹⁰. ¹Rheumatology and Rehabilitation, School of Medicine Tanta University, Tanta, Egypt; ²Rheumatology, Darent Valley Hospital, Dartford, UK, Dartford, United Kingdom; ³Rheumatology and Rehabilitation, School of Medicine Zagazig University, Zagazig, Egypt; ⁴Rheumatology and Rehabilitation, School of Medicine Banha University, Banha, Egypt; ⁵Rheumatology and Rehabilitation, School of Medicine Cairo University, Cairo, Egypt; ⁶Rheumatology and Rehabilitation, School of Medicine Assiut University, Assiut, Egypt; ⁷Rheumatology and Rehabilitation, School of Medicine Suez Canal University, Ismailia, Egypt; ⁸Pediatrics, School of Medicine Cairo University, Cairo, Egypt; ⁹Pediatrics, School of Medicine Alexandria University, Alexandria, Egypt; ¹⁰Rheumatology and Rehabilitation, School of Medicine Ain Shams University, Cairo, Egypt; ¹¹Community and Public Health, School of Medicine Ain Shams University, Cairo, Egypt

Background: The management of rheumatoid arthritis has evolved in the last few years with greater emphasis on a treat-to-target strategy rather than specific drug regimens. Technologies such as ultrasound have been increasingly used for diagnosis and monitoring of synovitis where it is unclear from clinical examination. These aspects of management were investigated by the Guideline Committee, and recommendations have been updated using new evidence [1, 2].

Objectives: To develop an updated evidence-based, interdisciplinary recommendations for the management of rheumatoid arthritis (RA).

Methods: The task force comprised rheumatologists, epidemiologists, health economists, and patients. A systematic literature analysis was conducted using the Cochrane Database of Systematic Reviews and MEDLINE. Data regarding the drugs prices and product information were collected to evaluate drug cost and safety. Evidence and recommendations were graded, and an algorithm for treatment and final statements were discussed in a consensus meeting (Nominal Group Technique). Recommendations were developed using a Delphi method by a multidisciplinary panel including patients.

Results: Consensus was reached on recommendations, including a standardized treatment strategy according to the RA severity, activity and prognostic factors in the individual patient. In this updated interdisciplinary guideline for RA the treat to target strategy was considered the cornerstone in these recommendations (figure 1). RA patients should reach clinical, ultrasonographic and functional remission. Treatment decisions should incorporate the disease activity status, structural damage progression (radiologic/sonographic), comorbidities, quality of life and patient motivation. Psychiatrist, psychologist and occupational therapist should be included in interdisciplinary treatment team for RA.

Conclusion: The treatment strategy included a total of twenty-one evidence based interdisciplinary recommendations for management of RA (figure 1), and is accompanied by a more in-depth discussion of key management principles. These recommendations provide a step-wise approach to treatment, to enable practitioners to develop and support the most effective method of achieving and maintaining remission in RA patients. These recommendations are not to remove the physician's autonomy, and physicians must select the most appropriate therapeutic option, taking into consideration the patient's preferences.

1. Treat-to-target strategies of RA aiming to reach sustained clinical remission (as defined by the American College of Rheumatology (ACR)-EULAR Boolean or index criteria) or low disease activity.
2. Implement communication, shared decision, self-management and education are very critical in treatment strategy.
3. Regular close monitoring of RA patients every 1-3 months then every 3-6 months after achieving treatment target to (assess disease activity and damage, functional ability, comorbidities and complications) is very important.
4. Ultrasonography has an important role in RA diagnosis, monitoring activity, damage and response to treatment.
5. Start the first line of treatment strategy with monotherapy using methotrexate. Shared decision making is advisable to agree which methotrexate administration form is preferable (oral Vs Subcutaneous Vs Intramuscular).
6. In patients with a contraindication to MTX or show intolerance to it, start leflunomide or sulfasalazine as first line of treatment strategy.
7. When the treatment target (remission or low disease activity) has not been achieved despite dose escalation by 3 months; adding another cDMARD or use combination cDMARD therapy.
8. Short-term glucocorticoids should be considered when initiating or changing cDMARDs.
9. Consider oral NSAIDs when control of pain or stiffness is inadequate, offer the lowest effective dose for the shortest possible time considering the comorbidities.
10. If the treatment target not achieved after 6 months of cDMARD combination therapy; addition of a bDMARD should be considered with or without MTX.
11. The cutoff point of starting biologic therapy is High Disease Activity: DAS-28 > 5.1, or if DAS-28 > 4.2 and associated with 3 or more poor prognostic factors.
12. First line biologic therapy: Use TNF-inhibitors or IL-6 inhibitor. TNF-inhibitors had been given a slight preference over other biologics due to availability of long-term registry data worldwide.
13. Significant improvement using bDMARDs should be achieved by 3 months and the target should be achieved by 6 months.
14. An alternative TNF α inhibitor may be considered for patients in whom treatment is withdrawn due to an adverse event.
15. If the patient has a primary failure to TNF α inhibitor, prescription of an alternative TNF α inhibitor is not advised. Switch out of therapeutic class considering a drug with other working mechanism.
16. In case of secondary failure to anti-TNF agent; adding a cDMARD or alternatively switch to another anti-TNF or switch to bDMARD with other therapeutic class of bDMARD.
17. A bio-similar (bsDMARD) of any of the reference bDMARDs should not be used if the respective bDMARD (or another bsDMARD of the same molecule) has failed to induce sufficient efficacy or vice versa.
18. If target not achieved after 6 months; treatment, change to a non-TNFi bDMARD (IL-6 inhibitors, rituximab or abatacept) with/without cDMARD.
19. If improvement still not achieved; try another bDMARD or use Targeted synthetic DMARDs tsDMARDs as JAK inhibitors (tofacitinib, baricitinib) or another non-TNFi bDMARD as third line bDMARDs till reach remission.
20. Non-pharmacological management (physiotherapy, occupational therapy, psychotherapy and nutritional advice) are important to improve functional, psychological and health status of RA patient.
21. Referral of RA patient for surgical opinion has certain time and indications for getting maximum benefits.

Figure 1: treat to target interdisciplinary guidelines for management of RA

REFERENCES:

- [1] Qiang Guo, et al. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. *Bone Res* 2018; 6: 15-21.
- [2] Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017; 76(6):960-977.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.2054

FRI0075

SYSTEMATIC ANALYSIS OF INJECTION-SITE PAIN CAUSED BY SUBCUTANEOUS ADMINISTRATION OF THE ADALIMUMAB BIOSIMILAR FKB327 VERSUS ADMINISTRATION OF THE ADALIMUMAB REFERENCE PRODUCT VIA DIFFERENT DELIVERY METHODS

Rieke Alten¹, Mark C. Genovese², Malcolm Boyce³, Takuma Yonemura⁴, Takahiro Ito⁵, Herbert Kellner⁶. ¹University Medicine Berlin, Berlin, Germany; ²Stanford University, Division of Immunology and Rheumatology, Palo Alto, CA, United States of America; ³Hammersmith Medicines Research, London, United Kingdom; ⁴Souseikai Sumida Hospital, Tokyo, Japan; ⁵Fujifilm Kyowa Kirin Biologics, Tokyo, Japan; ⁶Specialist Practice in Rheumatology and Gastroenterology, Munich, Germany

Background: FKB327 is a proposed biosimilar of the adalimumab reference product (RP). Several studies in both healthy volunteers and patients with active rheumatoid arthritis (RA) were undertaken, the results of which have been reported elsewhere. The formulation excipients of the biosimilar product differ from those of the RP, and different injection-site pain intensity with subcutaneous injection has been reported.

Objectives: The current meta-analysis examines pooled data from these studies in relation to the amount of injection-site pain resulting from using a prefilled syringe (PFS) versus an auto-injector (AI) versus a regular syringe (RS), and the proposed biosimilar, FKB327, versus the RP.

Methods: Data from 4 studies, FKB327-001, -002, -003, and -004, were pooled in an effort to compare injection-site pain upon subcutaneous administration of FKB327 versus the RP (citrate-containing formulation of the RP [40 mg/0.8 mL]). Study FKB327-001, in healthy volunteers (n =

180), involved a single subcutaneous dose of either FKB327 or the RP. Study FKB327-004 was a similar study in healthy Japanese volunteers (n = 130). Study FKB327-002 was a randomized (FKB327 with RS or the RP), double-blind, multiple-dose study in patients with active RA. This was followed by Study FKB327-003, in which patients were randomized to receive either FKB327 with PFS or the RP in the randomization phase, followed by an open-label extension phase of the study, in which AI was introduced. As patients continued receiving treatment or switched treatments during the course of the FKB327-002 and -003 studies, injection-site pain was assessed at the first dosing occasion of FKB327 or the RP (n = 691). Data from all 4 studies were examined by meta-analysis of the visual analog scale (VAS) using a 100-mm horizontal scale for FKB327 versus the RP and for comparison of AI, PFS, and RS.

Results: Data were analyzed from a total of 2007 assessments in 1001 subjects. A linear mixed model of the VAS in mm for the RP versus FKB327 across all 4 studies showed a 12.6-point lower pain score for FKB327 versus the RP (95% confidence interval [CI], -14.3 to -10.8; $P < .001$). For the AI and PFS used for FKB327 administration, AI showed a 1.7-point lower pain score in the VAS compared with PFS (95% CI, -3.3 to -0.1; $P = .035$). Gender, age, body weight, and population (healthy subject or patient) were not identified for differences in injection-site pain intensity.

Conclusion: FKB327 showed a significant advantage in terms of injection-site pain intensity compared with the RP, as well as lack of inferiority for both AI and PFS versus RS.

Disclosure of Interests: Rieke Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, Mark C. Genovese Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RPharm, Consultant for: Sanofi/Genzyme, Genentech/Roche, RPharm, Malcolm Boyce: None declared, Takuma Yonemura Grant/research support from: I have received a research grant from FKB for conducting the clinical study., Takahiro Ito Employee of: I am an employee of Fujifilm Kyowa Kirin Biologics., Herbert Kellner Grant/research support from: Roche, Consultant for: Roche

Figure 1. Forest Plot of Mean Treatment Difference and 95% CI of VAS (mm) Subgroup Analyses of Injection-Site Pain Data Collected Immediately After Injection at Day 1

DOI: 10.1136/annrheumdis-2019-eular.1292

FRI0076

THE RISK OF TUBERCULOSIS IN PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISORDERS RECEIVING BIOLOGICAL THERAPY: A 15-YEAR EXPERIENCE IN A ROMANIAN COHORT

ANCUTA CODRINA^{1,2}, Cristina Pomirleanu^{1,2}, Georgiana Strugariu¹, Luiza Petrariu¹, Raluca Paiu¹, Eugen Ancuta³, Codruta Bran⁴, Rodica Chiriac⁵. ¹Clinical Rehabilitation Hospital, Iasi, Romania; ²Grigore T Popa University of Medicine and Pharmacy, Iasi, Romania; ³Elena Doamna Clinical Hospital, Iasi, Romania; ⁴Stantul Ioan cel Nou Emergency Clinical Hospital, Suceava, Romania; ⁵SANOCARE Medical and Research Center, Iasi, Romania

Background: The risk of tuberculosis (TB), either reactivation of latent TB or *de novo* infection, remains a point of interest in patients with immune-mediated rheumatic pathology on biological therapy, particularly TNF α inhibitors.

Objectives: We aimed to evaluate the risk and to identify predictors for TB in biologics users among patients with rheumatoid arthritis (RA),