FRI0074

FACTORS ASSOCIATED WITH THE DEVELOPEMENT OF SEVERE RESPIRATORY INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS INCLUDED IN A VACCINATION PROGRAM

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Background: Rheumatoid arthritis (RA) patients are at increased risk of severe infections. Besides the disease itself, the immunosuppressive treatment appears to play an important role in the risk of infections. Vaccination programs are designed to decrease the risk of infections in these patients.

Objectives: Our aim was to assess the incidence of severe respiratory infections in patients with RA and to determine the underlying risk factors for the development of these complications.

Methods: Retrospective study of 401 patients diagnosed with RA who were invited to participate in a vaccination program from October 2011 to October 2016. The follow-up was made until June 2017 with a minimum follow-up period of 8 months and maximum of 5.5 years.

Information on severe respiratory infection episodes was retrieved from the hospital medical records. Serious infections were defined as those that required hospitalisation or at least one dose of intravenous antibiotic treatment at the emergency room.

Only 7 patients refused vaccination (2%). Information was not obtained in 4 of the remaining 394 patients. Therefore, these 4 patients were not included in the assessment.

Results: 390 patients (307♀/83 ♂) average age 61.28±12.9 years were vaccinated a followed-up. The main features at the time of vaccination were: median disease duration (4 years), positive rheumatoid factor (56.7%), subcutaneous nodules (4.9%), erosive arthritis (36.9%), pulmonary fibrosis (3.8%), Sjögren syndrome (5.1%) other extraarticular manifestations (14.6%) and rheumatoid vasculitis (5.6%). Most patients had received immunosuppressive drugs before the vaccination program. The most frequently used were systemic corticosteroids (n=228), methotrexate (n=362) and biologic agents (40.3%).

During the follow-up, 42 patients (10.7%) had required hospital admissions due to infections, 17 of them were severe respiratory infections (4.35%) The remaining 25 admissions were in the setting of urinary tract infections (n=12), intraabdominal infections (n=7), skin and soft tissues (n=12) and articular (n=1). Also 12 of these patients had a zoster herpes.

The presence of anti-citrullinated protein antibodies (ACPA) was associated with an increased frequency of admissions due to these infections. It was also the case for the presence of a history of biologic therapy prior to vaccination. No association of severe respiratory infection with rheumatoid factor, erosions or pulmonary fibrosis was found. (table 1).

Abstract FRI0074 – Table 1

Admission for severe respiratory infections	Crude OR (CI 95%)	p	Adjusted OR* (CI 95%)	p
RF positivity	2.13 (0.67-6.83)	0.2011	2.26 (0.69-7.84)	0.1799
ACPA positivity	3.73 (1.04-13.43)	0.0441	4.49 (1.2-16.83)	0.0259
Erosions	2 (0.71-5.64)	0.1898	2.16 (0.75-6.25)	0.1573
Rheumatoid vasculitis	1.48 (0.40-5.42)	0.5527	1.38 (0.37-5.22)	0.6336
Pulmonary fibrosis	4.27 (0.87-20.91)	0.2932	2.45 (0.46-13.05)	0.2932
Biologic treatment before vaccination	3.02 (1.01-9.02)	0.0476	2.61 (0.85-8.07)	0.0947

*adjusted by age and sex.

Conclusions: Vaccinated patients with RA present a low incidence of severe respiratory infections. Positivity for ACPA and the use of biologics prior to vaccination are associated with increased risk of severe respiratory infections in these patients. Therefore, vaccination should be performed prior to the onset of biologic treatment.

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FRI0075

RISK OF HEPATITIS B INFECTION REACTIVATION IN RHEUMATIC DISEASES PATIENTS TREATED WITH ANTI-CD20 THERAPY

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Background: It has been widely established that the risk of hepatitis B reactivation is high in haematological patients receiving ANTI-CD20 therapy. For these patients the use of prophylaxis with antiretroviral drugs is recommended, and the same approach is also advocated in patients affected with rheumatic diseases, although the real risk seems to be lower.

Objectives: To evaluate the risk of HBV infection reactivation in patients with rheumatic diseases undergoing treatment with ANTI-CD20 therapy.

Methods: Retrieved data including demographical, therapeutic and clinical features as well as serological data were collected in 92 patients with different rheumatic diseases who underwent treatment with ANTI-CD20 from January 2009 to December 2016. Occult HBV infection at baseline (HBsAg negative, anti-HBcAg positive with or without anti-HBsAg and undetectable HBV-DNA) was observed in 25 patients (18 rheumatoid arthritis, 4 vasculitis, 2 systemic sclerosis and 1 dermatomyositis), none of them was treated with antiretroviral prophylaxis. HBV-DNA value was recorded at least every year, whereas HBsAg together with anti-HBsAg every six months and ALT every three months.

Results: During the whole observation period (mean time 39.28±26.6 months) none of the 25 patients (mean age 58.64±8.58 years; 68% women) had hepatitis B reactivation or HBsAg seroreversion. During the evaluated period 2 patients dropped out therapy, 1 stopped treatment for adverse event and 1 for ineffectiveness. After 70 months of therapy 1 patient presented low fluctuation of HBV-DNA title (13 IU/ml), that spontaneously returned negative after 3 months without therapeutic changes. In addition 1 patients shown an ALT increase unrelated to HBV reactivation.

Conclusions: In line with previous data, our experience suggests that the risk of hepatitis B reactivation in rheumatic patients undergoing treatment with ANTI-CD20 combined with sDMARD is very low. The regular monitoring of transaminases and hepatitis markers (HBsAg, antiHBsAg and HBV-DNA) during treatment has to be preferred to universal prophylaxis.

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FRI0076

CHRONIC WIDESPREAD PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SEVEN YEAR FOLLOW-UP OF PAIN DISTRIBUTION AND FACTORS FOR IMPROVEMENT

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Background: The knowledge of chronic widespread pain and factors associated to improvement of pain in patients with RA is sparse, in particular regarding longitudinal studies.

Objectives: To describe the change of pain distribution reports over time and to identify factors that predict improvement from chronic widespread pain in patients with RA.

Methods: Two postal questionnaires were sent out to patients included in the BARFOT (Better anti-rheumatic pharmacotherapy) study, the first in 2010 and the second in 2017. The questionnaire included a pain mannequin, NRS scales of pain, patient global assessment (PatGA) and fatigue, health assessment questionnaire (HAQ), health related quality of life measured by EQ-5D and patient reported BMI and 28-joint count of tender (TJC) and swollen joints (SJC). The responders to both questionnaires were divided into 3 groups according to the reported pain duration and distribution at each time point— patients having no chronic pain (NCP), chronic widespread pain (CWP), and chronic regional pain (CRP).

Results: 1525 (73%) patients answered the pain questions in 2010 and 1046 (68%) in 2017. In all 950 of the patients answered the questions at both time points and were included in the study. One third (324) of the patients had reported CWP in 2010 and 140 (43%) of the patients with CWP in 2010 had improved in 2017. The patients, who improved, had lower BMI, $p=0.045$, less tender joint counts, $p=0.007$, less pain, $p=0.005$, less fatigue, $p<0.001$ and less painful regions, $p<0.001$, better PatGA, $p=0.002$, better HAQ, $p<0.001$ and better EQ-5D, $p=0.003$. Fifty-five percent of the patients who improved were treated with DMARD, compared to 52% of those not improving, the rate treated with biologics were 32% vs. 26%. There were, however, no statistical significant difference in medical treatment between the groups, $p=0.088$.

Age and sex adjusted logistic regression models showed an increased chance for improvement from CWP in patients with normal BMI, less TJC, pain, fatigue and tender regions and better PatGA, HAQ and EQ-5D, table 1. Biologic treatment also increased the chances to improve from CWP. The most common biologic treatment was anti-TNF treatment. Of the patients, who were treated with biologics, 86% in the group, who improved from CWP and 74% in the group, who did not improve, were treated with anti-TNF treatment. Age, gender, smoking habits, SJC and glucocorticoid treatment were not associated with improvement in the model.

Abstract FRI0076 – Table 1. A crude logistic regression model were the data were age and sex adjusted, except age, which was adjusted for sex and sex, adjusted for age.

	OR	95% CI
Age 2010	1.011	0.992-1.031
Gender		
women	0.960	0.542-1.702
Smoking habits 2010		
Smoker	0.580	0.282-1.195
Previous smoker	0.793	0.479-1.311
BMI 2010		
<18,5	0.320	0.037-2.930
18,5-24,9	2.146	1.121-4.106
25-29,9	1.294	0.708-2.365
TJC 2010	<7	1.798
SJC 2010	<4	1.477
PatGA 2010	<4	1.806
Pain 2010	<5	1.836
Fatigue 2010	<6	3.249
EQ5D 2010	≥0.725	2.092
HAQ 2010	<0.75	1.988
Total pain regions 2010	<8	2.987
Medical treatment 2010		
DMARD	1.779	0.940-3.366
Biologics	2.202	1.099-4.413
Prednisolone treatment 2010	Pred	0.753
		0.448-1.265

Conclusions: Lower scores in pain related variables and fatigue, normal BMI, better physical function and health-related quality of life, and biologic treatment were associated to improvement from CWP in patients with RA. Knowledge of factors associated to improvement from CWP could be helpful when treating RA patients with CWP. More studies with focus on improvement from chronic pain in patients with RA are needed.

Disclosure of Interest: None declared

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FRI0077

HEPATITIS B VIRUS REACTIVATION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB: POST-HOC ANALYSIS FROM CLINICAL TRIALS

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Background: Baricitinib (BARI) is an oral selective Janus kinase (JAK)1 and JAK2 inhibitor approved in the EU, Japan, and other countries for treatment of moderately to severely active rheumatoid arthritis (RA) in adults. RA therapies may increase risk of hepatitis B virus (HBV) infection¹. HBV reactivation is a concern in previously infected patients (pts), including those with serologic evidence of resolution. HBV exposure is common in many Asian countries.² Limited data exist on HBV reactivation among pts with RA treated with JAK inhibitors.

Objectives: To assess HBV reactivation in pts with RA treated with BARI during Phase (Ph) 3 trials.

Methods: At screening, all pts were tested for HBV surface antigen (HBsAg), core antibody (HBcAb) and surface antibody (HBsAb). In Japan and elsewhere if required, pts had screening HBV DNA tests. Pts were excluded if they had 1) HBsAg+, 2) HBcAb+/HBsAb- (in Japan, could enrol if HBV DNA-), or 3) HBsAb+ and HBV DNA+. Routine HBV DNA monitoring was performed in Japan for pts with HBcAb+ and/or HBsAb+ at screening, and was later instituted globally for HBcAb+ pts. Pts with post-baseline HBV DNA+ (≥ 29 IU/mL) were discontinued from the study and referred to a hepatologist. In select cases, investigators continued study drug following a HBV DNA+ test in consultation with the sponsor and in accordance with HBV management guidelines. Data were integrated from 4 completed Ph 3 trials and 1 ongoing long-term extension (LTE) (data to April 2017).

Results: Of 2890 pts with ≥ 1 dose of BARI (6993 pt-years exposure), 269 pts had baseline serology suggestive of prior infection (HBcAb+/HBsAb+, $n=255$; HBcAb+/HBsAb-, $n=14$) (figure 1). Post-baseline HBV DNA tests were performed for 290 pts (including some pts without a baseline HBV DNA result). After BARI initiation, 7 of 201 pts (3%) with HBcAb+/HBsAb+ at baseline had quantifiable HBV DNA+ levels (≥ 29 IU/mL; median 256, range 31–1547 IU/mL). An additional 23 (11%) had qualitative HBV DNA+ results below the lower limit of detection (LLD) (<29 IU/mL). Of these 30 HBcAb+/HBsAb+ pts with HBV DNA+ tests post-baseline, 22 had HBV DNA- tests at baseline. Among 14 pts with HBcAb+/HBsAb-, all had HBV DNA- tests at baseline; repeat HBV DNA test results post-baseline were quantifiable (1 at 36 IU/mL), below the LLD,¹ and undetectable.¹² Of pts with quantifiable HBV DNA, adverse events (AE) of detectable HBV DNA resulted in discontinuation of 4 of 8 pts of whom 3 received antivirals. 4 of 8 pts continued BARI in the LTE and have not received antivirals. All pts with quantifiable HBV DNA had alanine transaminase (ALT) or aspartate transaminase (AST) within normal limits, and none had an investigator-reported AE of hepatitis.

HBV serology and DNA detectability in patients treated with baricitinib in Phase 3 trials

*Total number of patients with baseline serology is $n=2881$ due to missing data for 9 patients (8 missing surface antibody and 1 missing core antibody data).

*Patients with detectable post-baseline HBV DNA were from China (11), Japan (9), Taiwan (6), Israel (2), Greece (2), Russia (2), United States (2), Argentina (1), and South Korea (1).

*Nine patients had quantifiable HBV DNA levels of 31, 36, 60, 76, 92, 256, 257, 869, and 1547 IU/mL.

*Patient with ALT/AST $\geq 3 \times$ ULN was discontinued from study due to abnormal liver function test. Patient had a single detectable HBV DNA test result <29 IU/mL. At last available observation, ALT and AST were $<3 \times$ ULN and $<2 \times$ ULN, respectively.

*Baseline HBV DNA not detected (5), not tested (2).

*Baseline HBV DNA not detected.

Abbreviations: AE=adverse event, ALT=alanine transaminase, AST=aspartate transaminase, BARI=baricitinib, HBcAb=hepatitis B virus core antibody, HBsAb=hepatitis B virus surface antibody, HBV=hepatitis B virus, DNA=deoxyribonucleic acid, Ph=phase, RA=rheumatoid arthritis, ULN=upper limit of normal.

Abstract FRI0077 – Figure 1. HBV serology and DNA detectability in patients treated with baricitinib in Phase 3 trials

Conclusions: Approximately 12% of BARI-treated pts with prior HBV infection later tested HBV DNA+ (3% were above the LLD), although no pts developed clinical evidence of hepatitis and in most cases antiviral therapy was not used.

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