FRI0117

INCIDENCE RATE OF HERPES ZOSTER IN RHEUMATOID ARTHRITIS PATIENTS UNDER TOFACITINIB: REAL-LIFE DATA FROM TURKEY – HURBIO REGISTRY

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Background: Tofacitinib (TOF) is an orally administered Janus Kinase (JAK) inhibitor and is commonly used in rheumatoid arthritis. There is a heterogeneity among numbers reported from different continents about herpes zoster (HZ) incidence rate (1-3). However, data about HZ risk in our country, which stands like a bridge between Asia and Europe, is lacking.

Objectives: To assess the real-life incidence of herpes zoster in RA patients under tofacitinib.

Methods: We analyzed all patients who had at least 1 control visit under tofacitinib and registered to HURBIO database. We calculated incidence rate by dividing the number of patients with herpes zoster to total follow-up years, then multiplied by 100 (per 100 patient-years).

Results: A total of 204 (174 (85.4%) female) patients were recruited. Mean age was 53.2±12.5 years. Mean disease duration was 11.5±8.1 years. Rheumatoid factor and anti-CCP antibodies were positive in 135/198 (68.1 %) and 115/171 (67.2 %) patients, respectively. Median follow-up while receiving TOF was 11.6 (IQR:5.2-26.2) months. Combination with DMARDs was used in 83.3% of patients. 55.5% of patients was biologic-naïve. Eleven (5.3%, incidence rate: 3.9 (2.3-8.5; % 95 CI) per 100 patient-years) patients had zona zoster. Ten of these patients was female, median age was 59 (IQR: 52-69) and 4 of them was older than 65 years-old. Rheumatoid factor was positive in 9 patients. Only 1 of these patients had diabetes. Median follow-up of these patients under TOF was 8.1 (IQR: 6-25) months. Ten of these patients had concomitant DMARDs (9 hydroxychloroquine, 4 methotrexate, 2 leflunomide; according to last follow-up visit) and 9 of them received concomitant steroids (med(IQR): 4 (1-8) mg- at equivalent methyl-prednisolon dose). Eight of them was biologic-naïve. Tofacitinib was discontinued in 4 of these patients.

Conclusion: In this real-life data from Turkey, we found a HZ incidence rate similar to that reported from USA and global data; however, we found a lower incidence rate that reported from Japan (Figure 1).

Figure 1. Reported herpes zoster incidence rates across different countries (numbers in paranthesis indicate reference number)

References:

- [1] Winthrop KL, Curtis JR, Lindsey S, Tanaka Y, Yamaoka K, Valdez H, et al. Herpes Zoster and Tofacitinib: Clinical Outcomes and the Risk of Concomitant Therapy. *Arthritis & rheumatology* (Hoboken, NJ). 2017;69(10):1960-8.
- [2] Curtis JR, Xie F, Yun H, Bernatsky S, Winthrop KL. Real-world comparative risks of herpes virus infections in tofacitinib and biologic-treated patients with rheumatoid arthritis. *Ann Rheum Dis*. 2016;75(10):1843-7.
- [3] Yamanaka H, Tanaka Y, Takeuchi T, Sugiyama N, Yuasa H, Toyozumi S, et al. Tofacitinib, an oral Janus kinase inhibitor, as monotherapy or with background methotrexate, in Japanese patients with rheumatoid arthritis: an open-label, long-term extension study. *Arthritis Res Ther*. 2016;18:34.

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FRI0118

RISK OF LIVER FIBROSIS ON TRANSIENT ELASTOGRAPHY IN PATIENTS WITH RHEUMATIC DISEASE UNDER LONG-TERM METHOTREXATE TREATMENT

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Background: Methotrexate (MTX) is a cornerstone drug for the treatment of rheumatic disease and low doses of MTX are both tolerable and safe, with monitored toxicity, assessed via the liver function test. However, there is still controversy regarding the risk of liver fibrosis with long-term use of MTX. Transient elastography is commonly used to assess and monitor fibrosis progression in patients with chronic liver disease.

Objectives: The present study aims to investigate liver fibrosis using transient elastography and related factors in patients with rheumatic disease receiving long-term MTX.

Methods: The present retrospective, longitudinal, cross-sectional study included patients with an autoimmune disease who are taking cumulative MTX dosed over 7 g, and who had liver fibrosis upon examination using transient elastography. Liver fibrosis was defined as liver stiffness, valued over 7.2 kPa. Logistic regression analysis was performed to identify factors associated with liver fibrosis, and receiver operating characteristics analysis was used to determine the predictive value of each factor.

Results: We included 83 patients with autoimmune disease, with a median MTX cumulative dose of 11.6 (range 7.3-16.0) g. Sixty-eight patients (81.9%) had rheumatoid arthritis (RA), and 13 patients (15.7%) had Takayasu arteritis. The median MTX exposure duration was 18 (range 9-31) years. The median liver stiffness value was 4 (range 1.8-10.2) kPa. Five patients (6%) showed liver fibrosis (3 patients; RA, 2 patients; Takayasu arteritis). In the linear regression analysis, cumulative MTX dose showed a tendency towards a positive correlation with increasing liver stiffness value ($r^2 = 0.039$, $p = 0.074$). In the logistic regression analysis, cumulative MTX dose was associated with a higher risk of liver fibrosis (OR: 1.734, 95% CI: 1.060–2.837, $p = 0.029$). In addition, cumulative MTX dose had an area under the curve (AUC) of 0.813 (95% CI 0.695–0.930) and a sensitivity of 80% and specificity of 71.8% at a cut-off value of 12.7 g.

Conclusion: Liver fibrosis was observed in 6% of patients with long-term MTX use and higher cumulative MTX doses increased the risk of liver fibrosis. Thus, transient elastography should be considered in patients exposed to high cumulative doses of MTX.

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FRI0119

TITLE USE OF JAK INHIBITORS IN THE TREATMENT OF RA PATIENTS IN THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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Background: JAK inhibitors are the newest therapeutic class available in Romania for the treatment of rheumatoid arthritis (RA). Both available JAK inhibitors (baricitinib and tofacitinib) are fully reimbursed.

Objectives: Efficacy and safety data for JAK inhibitors, derived from the Romanian Registry of Rheumatic Diseases (RRBR).

Methods: cohort retrospective study, the data being gathered from RRB, which includes all the patients treated with biologics and targeted synthetic DMARDs in the country. Inclusion criteria: at least one treatment course of JAK inhibitors, until end of 2019. The collected data: demographic and disease characteristics, efficacy parameters (DAS28) and safety data (exposure to JAK inhibitors in person-years (PY) and reported adverse events (AE)).

Results: the RA cohort treated with JAK inhibitors included 416 patients (7.6% of all RA patients registered in RRB) exposed to baricitinib (306 pts) or tofacitinib (110 pts) for 66255 PY. The mean age was 57.91 years, 365 (88%) women, 41 (10%) smokers, mean RA duration 11.32 years, 316 (76%) RF positive, 254 (61%) ACPA positive, 356 (85.5%) patients associate a synthetic DMARD, 76 (18%) use steroids (66% <7.5mg prednisone/day); 268 (65%) patients have cardiovascular comorbidities, 84 pts (20%) have modified lipid profile, 89 patients (21.4%) have latent TB, 86 (20.7%) have resolved HBV infection state. JAK inhibitors were the first treatment option for 178 patients (43%), all other patients have been exposed previously to at least one TNF-inhibitor or a biologic with another mode of action, being insufficient responders, as follows: 96 patients – to 1 biologic, 80 patients – to 2 biologics, 30 patients – to 3 biologics, 23 patients – to 4 biologics, 8 patients – to 5 biologics and 1 patient - to 7 molecules before the JAK inhibitors start. Of all patients exposed to JAK inhibitors, 252 (60.5%) patients have continued the therapy since the start summarising 61481PY of exposure. The efficacy parameters reported to this category revealed a mean DAS28 score of 3.08, significantly lower compared to 6 months before (4.77). Regardless the number of biologic agents used before starting a JAK inhibitor, there is no significant difference in DAS28 score when comparing it with DAS28 efficacy of the first treatment option scenario (3.10 vs 2.94, $p > 0.05$). Steroid use, the presence of RF or disease duration have no influence on the efficacy DAS28. On contrary, the ACPA positivity subgroup has a significantly lower DAS28 score, compared to ACPA negativity (3.18 vs 3.82, $p < 0.05$); smoker status has a significantly higher DAS28 compared to non-smokers (3.58 vs 2.94, $p < 0.05$). A total number of 46 AEs were reported for a total exposure of 66255PY. Infections were the most frequently reported AE (0.04/100PY, with 27 events); 6 cases of herpes zoster infection (0.009/100PY, all mild); 3 MACE (0.004/100PY). There were 3 severe adverse events (0.004/100PY) (1 hepatitis non-viral, 2 MACE) with one fatal (acute myocardial infarction).

Conclusion: JAK inhibitors represent a safe and efficacious treatment option for patients with active RA.

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FRI0120

ORAL GLUCOCORTICOID USE IS ASSOCIATED WITH HYPERTENSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Oral glucocorticoids (GC) are frequently prescribed to patients with rheumatoid arthritis (RA), however GC use is associated with a number of potential side effects. Hypertension is cited as a possible side effect, but few studies have specifically investigated GC-associated hypertension in patients with RA with conflicting results.

Objectives: The aim of this study was to determine whether GCs were associated with an increased risk of incident hypertension in a cohort of patients with RA.

Methods: A retrospective cohort of patients with incident RA and no hypertension at RA diagnosis were identified from UK primary care electronic health records (Clinical Practice Research Datalink). GC prescriptions were used to determine time-varying GC use and dose, categorised as: no use, >0–4.9mg/day, 5–7.4mg/day, 7.5–14.9mg/day, ≥15mg/day. A 3-month risk attribution model was used where patients continued to remain at risk for 3 months after the end of prescriptions. Hypertension was identified if a patient had either: 1) 2 consecutive systolic blood pressure (BP) measurements >140mmHg within a year, 2) 2 consecutive diastolic BP measurements

>90mmHg within a year or 3) antihypertensive prescriptions on at least two occasions and a Read code for hypertension. Unadjusted and adjusted Cox proportional hazards (PH) regression models were fitted to determine if there was an association between GC use and hypertension. Models were adjusted for baseline age, gender, baseline body mass index, baseline ever smoking, time-varying synthetic disease-modifying anti-rheumatic drug use, time-varying non-steroidal anti-inflammatory drug use and baseline Charlson comorbidity index.

Results: There were 17,760 patients with incident RA and no hypertension. The cohort had a mean age of 56.3 ± 12.7 years and were predominantly female (68%). 7,421 (42%) were prescribed GCs during follow-up. There were 6,243 cases of incident hypertension over 97547 person years (pyrs) of follow-up, giving an incident rate of 64.1 per 1000 pyrs. Of those 1321 cases were in those exposed to GCs and 4922 were in those unexposed, giving incident rates of 87.6 per 1000 pyrs and 59.7 per 1000 pyrs, respectively. The adjusted Cox PH model indicated that recent GC use was associated with a 17% increased hazard of hypertension (hazard ratio: 1.17 (95% CI 1.10 to 1.24)). When categorised by dose, the adjusted model indicated only doses above 7.5mg were significantly associated with hypertension (Table 1).

Table 1. Unadjusted and adjusted Cox proportional hazards regression model results

	Unadjusted HR (95% CI)	Age and gender adjusted HR (95% CI)	Fully adjusted* HR (95% CI)
Recent GC use	1.44 (1.35 to 1.53)	1.23 (1.16 to 1.31)	1.17 (1.10 to 1.24)
Recent GC dose	Reference	Reference	Reference
No GC use	1.35	1.13	1.10
>0 – 4.9mg	(1.21 to 1.53)	(1.01 to 1.28)	(0.98 to 1.24)
5mg – 7.4mg	1.40 (1.22 to 1.60)	1.11 (0.97 to 1.27)	1.07 (0.93 to 1.23)
7.5mg – 14.9mg	1.44 (1.33 to 1.57)	1.26 (1.16 to 1.38)	1.18 (1.08 to 1.29)
15mg and over	1.60 (1.40 to 1.84)	1.45 (1.27 to 1.66)	1.36 (1.18 to 1.56)

* Adjusted for: Baseline age, gender, baseline body mass index, baseline ever smoking, synthetic disease-modifying anti-rheumatic drug use (time-varying), non-steroidal anti-inflammatory drug use (time-varying) and baseline Charlson comorbidity index.

Conclusion: In this large cohort of patients with RA and without hypertension, recent GC use was associated with incident hypertension. In particular doses ≥7.5mg were associated with hypertension while the association with lower doses was inconclusive. Clinicians need to consider cardiovascular risk when prescribing GCs and ensure BP is regularly monitored.

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FRI0121

STERIOD-SPARING EFFECT OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS FOLLOWED UP IN A REAL LIFE SETTING

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Background: Glucocorticoids (GCs) are a milestone of Rheumatoid Arthritis (RA) treatment; EULAR recommendations on the management of medium to high dose glucocorticoids remind to evaluate comorbidities and risk factors for adverse events when planning GCs treatment. Tofacitinib and Baricitinib are Janus kinases inhibitors (JAKi) registered for RA treatment. About 60% of patients enrolled in randomized clinical trials with JAKi were co-treated with GCs; however, little is known about tapering and percentage of withdrawal both in clinical trials and real life.

Objectives: To evaluate the steroid-sparing effect of JAKi in patients with RA.

Methods: We prospectively enrolled consecutive adult patients with RA starting JAKi. At baseline and after 4, 12 and 24 weeks we calculated C-Reactive Protein based Disease Activity score 28 (DAS28_{CRP}). Daily dose of GCs was recorded at each visit as prednisone (PDN)-equivalent dose. Data are expressed as median (IQR). Continuous variables were compared by Mann Whitney test while dichotomous ones by Chi-square test. P values < 0.05 were considered statistically significant.

Results: Between January 2018 and January 2020, 108 patients started JAKi: 67 patients Baricitinib, 41 patients Tofacitinib. The analysis was restricted to 64 RA patients (50 female, 14 male) who had at least 6 months of follow-up. Table 1 shows the demographic, clinical and clinimetric characteristics of the cohort.