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AB0362 HERPES ZOSTER IN BARICITINIB-TREATED JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS USING REAL-WORLD CLINICAL DATA

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Background: Similar to biologic disease-modifying anti-rheumatic drugs, the association between Janus kinase (JAK) inhibitors and infection is particularly interesting. The incidence of herpes zoster (HZ) among patients treated with JAK inhibitors is twofold to threefold higher in several regions of Asia (e.g., Japan and Korea) as compared with that observed in North America and Western Europe [1].
Objectives: To evaluate the characteristics of patients who developed HZ during baricitinib treatment using real-world, multicenter, clinical data for Japanese population.
Methods: The study enrolled 97 patients with rheumatoid arthritis (RA) who were treated with baricitinib therapy (68 biologic-naïve patients and 29 biologic-experienced patients) were enrolled in the study (observation period: 2–27 months). The severity of HZ infection was determined based on the extent of the rash and the presence or absence of organ damage. We evaluated the characteristics and clinical courses of patients who developed HZ.
Results: Eight patients with HZ. The incidence ratio (IR) was 8.2 per patient-year. Patient data are described in Table 1 and Table 2. The IR was a little higher than that reported in clinical trials [2], which could be attributed to the high average age (i.e., 67.3 years) of the patients in this study. It was reported that adverse events occurred more frequently in elderly patients aged ≥65 years compared with younger patients [3]. The period from baricitinib administration to the onset of HZ varied between 2 months and 16 months. It is suggested that HZ may develop at any time during baricitinib therapy. There were no distinctive patient characteristics, except for age, at the time of initial baricitinib administration between patients who developed HZ and those who did not.

Table 1. Characteristics of patients who developed HZ at initiation of baricitinib

Case-No.	Age (years)	Time (years) from RA onset	Gender Female:F Male: M)	BMI	Bari dose (mg/d)	PSL(mg/d)	MTX (mg/w)	HZ history	Number of prior biologics
1	74	1.5	F	25.6	4	0	12	No	2
2	61	33	F	19.2	2	0	6	No	1
3	61	11.1	F	23.6	4	0	10	Yes	0
4	73	0.5	M	23.3	4	0	8	Yes	0
5	74	21.9	F	20.9	2	0	0	No	0
6	78	1.2	F	19.8	4	0	6	No	0
7	48	23.2	F	24.1	4	4	8	No	0
8	79	5.0	F	22.4	2	2.5	4	No	0

Table 2. Clinical coutcome of patients who developed HZ at initiation of baricitinib

Case No.	HZ incidence period after baricitinib administration (months)	Priod of baricitinib withdrawal (weeks)	Severity (Mild; Mil Moderate: Mod)
1	16	4	Mod
2	2	4	Mod
3	13	1	Mil
4	3	1	Mil
5	8	6	Mod
6	3	4	Mil ~ Mod
7	3	3	Mod
8	20	Discontinuation due to pateient's choice	Mod

None of the patients had severe symptoms, and none of them experienced organ damage. All patients were cured with anti-viral agents. It should be noted that patients who had a history of HZ had milder symptoms than those who had no history of HZ. We noted an interesting finding in one patient (case 2). The half-life of baricitinib in the blood was very short (about 6 hours), and it is reported that the drug is almost fully excreted from the body 24 hours after its administration [4]. However, this patient developed an incidence of HZ at 17 days after the withdrawal of baricitinib for surgery management. Cells may take longer time to regain their original immune status even after excretion of the drug, especially, during intense stress such as in cases of surgical invasion.
Conclusion: The HZ risk in Japanese patients with RA treated with baricitinib in real-world practice was high, especially in elderly patients. It is notable that HZ events were nonserious and that patients could restart baricitinib treatment after healing with antiviral therapy, for the most part.
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AB0363 SAFETY OF JAK INHIBITORS IN PATIENTS WITH ARTHRITIS RHEUMATOID UNDER REAL-LIFE CONDITIONS

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Background: Efficacy and safety profile of new JAK inhibitors have been properly defined by several clinical trials, being tested in many patients with Arthritis Reumatoid. However, real-life conditions studies play an important role in order to know JAK inhibitors behaviour in safety.
Objectives: To describe adverse events of JAK inhibitors in patients with Arthritis Rheumatoid and asses the survival in relation to adverse events.
Methods: Observational, descriptive, retrospective design performed in patients with Arthritis Reumatoid in follow-up by the Rheumatology department of the Hospital de Valme until January 2019. Demographic and clinical data related to safety has been collected
Results: 58 patients were included with a mean age of 57,77 ± 10,78 years. Mean time from diagnosis was 8,7 ± 6,54 years, female predominance (75%). Mean ASDAS at the beginningof JAK inhibitor treatment was 4,76 ± 0,93. Regarding the determination of FR and CCCP 69% and was positive in both cases. Baricitinib was the treatment chosen in 13 patients (22.4%), and Tofacitinib in 45 patients (77.6%). Regarding associated treatments: 84.5% was under low-dose steroids theraphy; 77.6% was under combined therapy with at least 1 DMARD; 15.5% with two of them. Metotrexato was used in 53,4% of patients, leflunomide in 19%, hydroxycloroquine in 13.8%, sulfasalazyne in 12.1%. 72,4% have been before under at least one biologic treatment (frequently antiTNF), 41,1% one of them, 15.5% two of them, 12.1% three and 1.7% four before starting Jak inhibitor therapy. Adverse events has been observed in 17 patients (13 from de Tofacitinib group -28.8%-, and 4 in the Baricitinib group -30.76%). The most common advers events were: herpes zoster infections (4 patients in Tofacitinib group), respiratory infections (3), urinary infections (2), cutaneous (3), caphalea (1), legs oedema (2), toxic hepatitis in 1 patient of Baricitinib group; pulmonary thromboembolism was observed in 1 patient of Tofacitinib group, and atrial fibrillation in other patients of that group. Treatment was interrupted in 24 of 58 patients (mean time 8.92 ± 5.14 months), 16 from Tofacitinib group (35.5% of patients with Tofacitinib) and 8 from Baricitinib group (61.15% of patients with Tofacitinib). In Tofacitinib group, 10 patients stopped therapy for inefficacy reasons and 6 for advers effects related. In Baricitinib group, 5 due to inefficacy, 2 to adverse effects and 1 to clinical remission.
Conclusion: Main adverse effect were mild-moderate infections (involving in-hospital treatment only in one Baricitinib group patient). One pulmonary thromboembolism has been detected in a hypertensive 70 years old patient, supporting the recent recommendation of avoiding these drugs in patients over 65 or with cardiovascular risk factors. It is remarkable low survival results due to inefficacy, that could be related to clinical profile of refractory patients in our study, and/or to the small sample that we describe.
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