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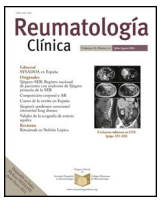

Letter to the Editor

Efficacy and safety of baricitinib in patients with rheumatoid arthritis and inadequate response to conventional synthetic DMARDs and/or biological DMARDs: Data from a local registry☆

Eficacia y seguridad de baricitinib en pacientes con artritis reumatoide y respuesta inadecuada a FAME convencionales sintéticos o biológicos: datos de un registro local

Dear Editor,

Intracellular JAK inhibitors (JAKi) are a new group of drugs, effective orally, for the treatment of rheumatoid arthritis (RA). They work at the intracellular level by inhibiting several group I and II cytokines.[1] Although, in general, the increase in infections is similar to that of other biological drugs, there appears to be a higher incidence of herpes zoster infection, in particular related to age and steroid treatment.[2]

Baricitinib (BARI) is a selective JAK1-JAK2 inhibitor that, when administered as a single daily dose, has been shown to be effective and safe in clinical trials in patients with RA who have not responded to conventional synthetic disease modifying drugs (csDMARDs) or biological drugs (bDMARDs).[3–7] However, there is little information in patients from clinical practice.[8–11]

The aim of this study, conducted in a real-life situation, was to determine the response to BARI in patients with inadequate response to csDMARDs or bDMARDs.

From October 2017 to June 2019 we collected patient characteristics (age, gender, comorbidity, BMI), characteristics of RA and of treatment when starting BARI and at the last recorded visit (disease duration, RF and ACPA, DAS28-ESR and CDAI, previous or concomitant treatment with FAMEcs or FAMEb, time on BARI, reason for discontinuation of treatment, severe adverse effects).

Of 230 RA patients in our centre who received a bDMARD or JAKi, 50 (22%) were treated with BARI. Eighty-four percent were female, with a mean age of 59 ± 10.5 years, the mean BMI was 28.3 ± 7 and mean duration of RA was 10.5 ± 8.5 years (range: 1-39 years). The RF and ACPA were positive at 80% and 82% respectively. Forty-seven (94%) patients received a concomitant csDMARD: methotrexate: 28 (56%), leflunomide: 15 (30%), hydroxychloroquine: 3 (6%), and salazopyrin: one (2%). At the start of treatment with BARI 23 (57%) patients were treated with prednisone daily (mean: 7.2 ± 4.7 mg; median: 5 mg; range: 2.5-20 mg).

BARI was the first drug after failure of a csDMARD (F1) in 27 (54%) patients, and after failure of a bDMARD in 23 (46%): the second drug (D2) in 4 (8%), third (D3) in 6 (12%), fourth (D4) in 8 (16%) and fifth (D5) in 5 (10%) patients.

Table 1
Patients treated with BARI as D1 or D2-D5: DAS28-ESR and mean CDAI baseline and at last visit. Ten patients were excluded: 8because they came from clinical trials and two due to treatment with BARI < 1 month.

	DAS28-ESR		*P*	CDAI		*P*
	Baseline	Last visit		Baseline	Last visit	
BARI D1	5.1	2.6	.0001	23.3	5.5	.001
BARI D2-D5	5.6	3.2	.0001	29.8	8.8	.001

For the analysis, during time under treatment with BARI, 10 patients were discarded: 8 because they came from clinical trials and 2 because they had been under treatment for less than a month, leaving 20 patients in the D1 group and 20 patients in the D2-D5 group. The overall average time on BARI was 9.6 ± 3.2 months, and D1, D2, D3, D4, D5, at 7.5, 7, 7.4, 7.7 and 11 months, respectively. The average time on BARI was 5.4 months. It was discontinued in 10/40 (25%) patients: in 5 (12.5%) patients due to loss of effectiveness, in 4 (10%) due to complications and in one (2.5%) patient due to transfer home.

When comparing patients treated with BARI as D1 versus group D2-D5, significant differences were detected in the mean duration of RA (7.1 ± 6.8 vs. 14.3 ± 8.5. *P* = .003). Of the D2-D5 patients, prior to starting on BARI, 9 (45%) D2 patients had failed to achieve one therapeutic target (TT), 8 (40%) D3 patients had failed to achieve 2 TT, and 3 (15%) D4-D5 patients had failed to achieve 3 TT. When comparing the results of DAS-ESR and CDAI from the baseline visit and the last visit, significant differences were obtained in all groups (Table 1).

BARI treatment was discontinued in 4 (20%) patients: 2 due to herpes zoster (one 58-year-old patient, on treatment with 2.5 mg of prednisone daily; one 71-year-old patient without corticoid treatment; both on methotrexate treatment at a dose of 15 mg weekly), one patient due to anaemia with haemoglobin less than 8 g/dL and the remaining patient due to increased transaminases, not controlled by reducing the BARI dose to 2 mg. During the time of the study, none of the patients presented a thrombotic event.

In this real-life study BARI was effective and safe. It can achieve clinical remission or low disease activity even in patients who have previously failed with various bDMARDs or several therapeutic targets. BARI losses of 20% in the first year of treatment usually occur in the first six months of treatment.

Conflict of interests

J Rosas has participated in consultancies with Janssen, Lilly and has received honoraria for talks from: Abbvie, Celgene, Lilly, MSD, Novartis, Pfizer. JM Senabre-Gallego has received honoraria for talks from: Janssen, Novartis, Pfizer. JA Bernal has received honoraria for talks from: Grünenthal, Pfizer. G Santos-Soler, has received honoraria for talks from: Grünenthal, Pfizer.

A Pons-Bas has no conflict of interests to declare.

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References

1. Bechman K, Subesinghe S, Norton S, Atzeni F, Galli M, Cope AP, et al. A systematic review and meta-analysis of infection risk with small molecule JAK inhibitors in rheumatoid arthritis. Rheumatology. 2019;58:1755–66.
2. Curtis JR, Xie F, Yang S, Bernatsky S, Chen L, Yun H, et al. Herpes Zoster in Tofacitinib: Risk is Further Increased with Glucocorticoids but not Methotrexate. Arthritis Care Res (Hoboken). 2019;71:1249–54.
3. O'shea JJ, Holland SM, Staudt LM. JAKs and STATs in immunity, immunodeficiency, and cancer. N Engl J Med. 2013;368:161–70.
4. Kubo S, Nakayamada S, Tanaka Y. Baricitinib for the treatment of rheumatoid arthritis. Expert Rev Clin Immunol. 2016;12:911–9.
5. Keystone EC, Taylor PC, Drescher E, Schlichting DE, Beattie SD, Berclaz PY, et al. Safety and efficacy of baricitinib at 24 weeks in patients with rheumatoid arthritis who have had an inadequate response to methotrexate. Ann Rheum Dis. 2015;74:333–40.
6. Genovese MC, Kremer J, Zamani O, Ludivico C, Krogulec M, Xie L, et al. Baricitinib in patients with refractory rheumatoid arthritis. N Engl J Med. 2016;374:1243–52.
7. Taylor PC, Keystone EC, Van Der Heijde D, Weinblatt ME, Del Carmen Morales L, Reyes Gonzaga J, et al. Baricitinib versus placebo or adalimumab in rheumatoid arthritis. N Engl J Med. 2017;376:652–62.
8. van Vollenhoven R, Helt C, Arora V, Zhong J, Correia AP, de la Torre I, et al. Safety and efficacy of baricitinib in patients receiving conventional synthetic disease-modifying antirheumatic drugs or corticosteroids. Rheumatol Ther. 2018;5:525–36.
9. Smolen JS, Genovese MC, Takeuchi T, Hyslop DL, Macias WL, Rooney T, et al. Safety profile of baricitinib in patients with active rheumatoid arthritis with over 2 years median time in treatment. J Rheumatol. 2019;46:7–18.
10. Tan J, Davies S, Linton S. E061. Retrospective cohort study of early real-life experience with baricitinib in rheumatoid arthritis. Rheumatology. 2019;58 Suppl 3, http://dx.doi.org/10.1093/rheumatology/kez110.059.
11. Fitton J, Dass S, Emery P, Nam J, Maya HB. 087. Janus kinase inhibitors demonstrate effectiveness in a real-world multi-biologic DMARD refractory rheumatoid arthritis population. Rheumatology. 2019;58 Suppl 3, http://dx.doi.org/10.1093/rheumatology/kez106.086.

José Rosas,[a,*] José Miguel Senabre-Gallego,[a,b,c] Gregorio Santos-Soler,[a,b,c] José Antonio Bernal,[a,b,c] Ana Pons Bas[a,b,c], Grupo Aire-Mb

[a] *Sección de Reumatología, Hospital Marina Baixa, Villajoyosa, Alicante, Spain*
[b] *Sección de Enfermedades Infecciosas, Hospital General Universitario de Elche, Alicante, Spain*
[c] *CIO-Universidad Miguel Hernández, Elche, Alicante, Spain*

* Corresponding author.
E-mail address: j.rosas.gs@gmail.com (J. Rosas).

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Increasing trend in mortality from systemic lupus erythematosus in Latin America as an expression of social disparities in health☆

Tendencia creciente en la mortalidad por lupus eritematoso sistémico en América Latina como expresión de las desigualdades sociales en salud

Dear Editor,

Despite the fact that in the last two decades diagnostic, therapeutic and preventative strategies regarding systemic lupus erythematosus (SLE) have improved, their impact on specific mortality from this disease is as yet unknown.[1,2] This has led to the use of data from mortality records to undertake cost-effective research studies with a standardised method on the epidemiological behaviour of mortality by SLE at a population level and over long periods of time.[1,3–5] The resulting evidence of these studies has helped to enhance the understanding of this disease and its recognition as a major health problem for healthcare authorities of several governments.[2,5,6] However, Latin America is experiencing a very different reality in political material and health reports regarding SLE.

Recently, Scherlinger M et al. published the worldwide trends on mortality from systemic autoimmune diseases during the period from 2001 to 2014 in the journal "*Autoimmunity Reviews*". For this they used the mortality database from the World health Organisation.[3] Their main conclusion was the standardised rate of mortality by SLE in Latin America was 5 times greater than that of Europe, a phenomenon which was not observed in the other systemic autoimmune diseases studied. Furthermore, during the 2003–2014 period, in Latin America and Asia, there was a significantly growing trend in standardised rates of mortality by SLE, whilst in Europe, North America and Oceania they demonstrated there was a decreasing trend and in Africa rates remained stable.[3] Posterior analysis by the same authors established an inverse correlation between countries' wealth and the standardized rate of SLE mortality.[1] These research studies confirmed the findings from 3 previous studies on this matter which were based on mortality records, with a similar methodology.[4,7,8]

Inequality dominates the American continent.[9] Against this backdrop, much discussion has arisen as to whether the greater severity and mortality observed in Latin American patients with SLE is a consequence of genetic factors or the expression of the influence on health of social determinants in which this patient group lives. The great majority of studies conclude that the main cause of these adverse findings are from the inequalities that affect minority groups where individual factors combine (poverty, malnutrition, lack of treatment compliance, adverse perception and non-adaptive behaviour related to the disease); factors affecting the health system (lack of access to specialised services, geographical isolation) and those caused by society (lack of social support, inadequate public policies and low gross domestic product).[2,10,11]

It is important to underline that the research studies mentioned share the inherent limitations of the mortality statistics of each country and do not offer information on the causes of death, disease activity or accumulated organ damage. Despite these methodological limitations, their findings are relevant because they identify the tip of the iceberg of this health problem in the region, and urge the Latin American scientific community to recognise and prioritise it.

Low regional evidence on the extension of the problem, its associated factors and the possible effective interventions to address it, are barriers which impede the right decisions being taken and

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