Treatment With Tofacitinib in Refractory Psoriatic Arthritis: A National Multicenter Study of the First 87 Patients in Clinical Practice

Eva Galíndez-Agirregoikoa, Diana Prieto-Peña, José Luis Martín-Varillas, Beatriz Joven, Olga Rusinovich, Rafael B. Melero-González, Francisco Ortiz-Sanjuan, Raquel Almodóvar, Juan José Alegre-Sancho, Ángels Martínez, Agustí Sellas-Fernández, Lara Ménendez, Rosario García-Vicuña, Belén Atienza-Mateo, Iñigo Gorostiza, Miguel Ángel González-Gay and Ricardo Blanco on behalf of the Tofacitinib PsA Clinical Practice Collaborative Group

The Journal of Rheumatology October 2021: https://doi.org/10.3899/jrheum.201204

Slide 1: Welcome to this video abstract. I am Diana Prieto-Peña from the Rheumatology Department of Marqués de Valdecilla University Hospital. I am glad to present today on behalf on my coauthors our paper entitled "Treatment with Tofacitinib in Refractory Psoriatic Arthritis. National Multicenter Study of the first 87 patients of clinical practice"

Slide 2: Psoriatic arthritis is a chronic inflammatory disorder comprising a wide spectrum of clinical domains, including skin and nail involvement, enthesitis, dactylitis as well as axial and peripheral arthritis. Tofacitinib is the first Janus kinase inhibitor approved for the treatment of PsA. OFA is a small-molecule inhibitor of JAK1, JAK3 and, to a lesser extent, JAK2 which inhibits key immune triggers of both psoriasis and PsA. In the OPAL Beyond trial, TOFA showed to be more effective than placebo in active PsA patients with an inadequate response to anti-TNFα. However, it is known that the demographic and clinical features of patients included in RCT may differ from those of clinical practice. These differences may have an influence on the clinical outcomes when applied to patients seen in daily clinical practice.

Slide 3: Taking all these considerations into account, our aim was to assess the efficacy and safety of TOFA in PsA patients from a real clinical setting with inadequate response and/or with unacceptable side effects to conventional therapy. In addition, we aimed to compare the clinical profile of patients from our cohort with those patients included in the OPAL BEYOND trial.

Slide 4: For this purpose, we conducted an open-label, multicenter study including 87 patients of clinical practice with refractory PsA treated with TOFA. PsA diagnosis was based on CASPAR criteria. Refractory PsA was defined when the patient did not achieve clinical low disease activity or remission despite the use of b-DMARDs or Apremilast. All patients were refractory to at least on cs-DMARDs and b-DMARDs, and in some cases to ts-DMARDs (apremilast). TOFA was used at the standard dose of 5 mg taken orally twice daily.

Slide 5: The outcome variable wee efficacy, sparing corticosteroid-dose effect, retention rate and safety to TOFA therapy. The main efficacy outcomes were improvement in the DAS28ESR and DAPSA. The secondary outcome was skin efficacy.

Slide 6: For the purpose of comparing the clinical profile of our cohort of patients with those from randomized clinical trial, information was retrieved from the results of the TOFA arm (5 mg/12 h) of OPAL BEYOND randomized clinical trial.

Slide 7: The outcome variables were assessed and compared between baseline (at TOFA onset), and at 1 and 6 months. Retention rate at month 6 was estimated using
Kaplan-Meier non-parametric survival data analysis in which the event was discontinuation of the drug due to inefficacy or toxicity. Analyses were performed using SPSS and Stata.

**Slide 8**: Results. Regarding baseline clinical features we studied 87 patients (28 women/ 59 men) with a mean age of 52.8 years. The pattern of joint involvement of PsA was peripheral (n=60), mixed (n=26) and axial (n=1). The mean±SD time from PsA diagnosis to TOFA onset was 12.3 years.

**Slide 9**: The main clinical features at the time of TOFA onset were arthritis in 95% of patients with a mean swollen joint count of 5.7 and a tender joint count of 8. Enthesitis was present in about 30% of patients and dactylitis in 18% of patients. Almost half of the patients had skin involvement with median PASI score of 5. CRP was elevated in 63.2% patients.

**Slide 10**: Before TOFA, all patients had received at least one conventional DMARDs and one biological DMARDs. The most common conventional DMARD was methotrexate, and the most common biological agents were etanercept, adalimumab and secukinumab. Apremilast was used in 17 patients.

**Slide 11**: TOFA was initiated at the standard dose of 5mg twice daily. Concomitant glucocorticoid therapy was administered to 50% of patients with a mean dose of Prednisone of 7.8 mg/day. Combined therapy MTX, LFN and SSZ was used in 48 cases. In the remaining 39 patients, TOFA was used as monotherapy.

**Slide 12**: Following TOFA therapy, patients experienced a rapid and maintained joint improvement. The main outcomes (DAS28ESR and DAPSA) showed a significant improvement at first month of TOFA that was longer maintained.

**Slide 13**: Likewise, PASI score showed a trend for improvement throughout follow-up, although no statistically significant differences were achieved. CRP decreased from a median of 1.9 to 0.5 mg/dL at the first month. A sparing corticosteroid-dose effect was also observed. TOFA led to a reduction of the prednisone dose from 7.8 to 6.6 at the first month.

**Slide 14**: As you can see the levels of hemoglobin, neutrophils, lymphocytes, and platelets maintained stable throughout follow-up. This was also the case for the renal and liver function. The lipid profile was also stable throughout follow-up.

**Slide 15**: Retention rate at month 6 was 77%. TOFA was discontinued in 29 patients after a mean follow-up of 6.5 months due to inefficacy in most cases.

**Slide 16**: Regarding adverse events, no serious adverse events were observed. 24.3% patients experienced at least 1 mild adverse event including gastrointestinal symptoms, urinary tract infection, cutaneous infection, upper respiratory tract infection, headache and sleep disturbances being the gastrointestinal symptoms the most common. No thrombotic events were observed, 3 patients presented mild lymphopenia and other 3 patients worsening of lipid profile.

**Slide 17**: In regard to the comparative study of clinical practice and the OPAL beyond trial Patients from our clinical practice cohort (n=87) were compared to those included in the arm with standard TOFA therapy (5 mg twice daily) of the OPAL BEYOND trial.
Slide 18: There was a higher proportion of men in patients from clinical practice. Also, they were older and had a longer PsA duration. A non-significantly increased functional disability was observed in patients from clinical practice.

Slide 19: In our series and had received a higher number of biological agents prior to TOFA than patients from OPAL BEYOND trial.

Slide 20: The tender and swollen joint count, PASI Score, as well as the proportion of patients with enthesitis and dactylitis, was higher in patients from the OPAL BEYOND trial.

Slide 21: Regarding treatment, patients in clinical practice required more frequently corticosteroids but less concomitant conventional DMARDs. In the OPAL BEYOND trial all patients received combined therapy with a stable dose of a single conventional DMARD whereas TOFA was used as monotherapy in 44 % of patients in our series.

Slide 22: In conclusion, data form clinical practice confirms that TOFA seems to be effective, rapid, and relatively safe in refractory PsA despite clinical differences with patients in clinical trials. Patients from clinical practice had a longer evolution of the disease and were more commonly refractory to conventional therapy. A corticosteroid dose-sparing effect was achieved. We observed a lower frequency of minor adverse events in comparison to the OPAL beyond trial and no serious adverse events were reported.