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INCIDENCE RATE AND CHARACTERIZATION OF HERPES ZOSTER IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS: AN UPDATE FROM BARICITINIB CLINICAL STUDIES

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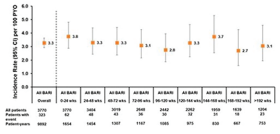
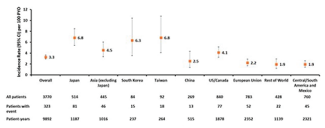
Background: Baricitinib (BARI) is a selective inhibitor of Janus kinase (JAK) 1 and JAK2, approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults in over 50 countries, including the United States, Europe and Japan. Due to their disease and associated therapy with disease-modifying anti-rheumatic drugs (DMARDs), RA patients (pts) have an increased risk of herpes zoster (HZ) compared with the general population.[1] Furthermore, the incidence of HZ is increased in RA pts treated with BARI versus placebo (PBO).[2]
Objectives: To determine the long-term overall and geographical incidence, time to first event and risk factors for HZ in BARI-treated RA pts.
Methods: Data were pooled from nine completed Phase 1, 2, and 3 studies of BARI in RA pts, including six randomised, PBO-controlled studies (0–24 weeks in DMARD-inadequate responders, including RA-BUILD, RA-BEACON and the long-term extension study, RA-BEYOND [data cut off February 13, 2018]), and active-controlled studies with methotrexate (MTX; RA-BEGIN study in DMARD-naïve pts) and adalimumab (RA-BEAM study in MTX-inadequate responders). The HZ incidence was evaluated for all RA pts who had ever received BARI (any dose) and the HZ incidence rate (IR) was calculated as the number of pts with an HZ event per 100 patient–years of observation (PYO). Exposure included up to 28 days after treatment cessation, and was censored at the HZ event date. Univariate and multivariate Cox proportional hazard regression models were used to evaluate risk factors for HZ.

Figure 1: HZ incidence rates per PYO over time



All BARI, all pts who had ever received BARI (any dose); BARI, baricitinib; CI, confidence interval; HZ, herpes zoster; PYO, patient–years of observation; wks, weeks.

Figure 2: HZ incidence rates per PYO by geographical region



CI, confidence interval; HZ, herpes zoster; PYO, patient–years of observation.

Results: Of 3770 RA pts treated with BARI, median age at study entry was 54 years (range 20–90 years), approximately one-quarter were each from North America (n=840; 22%), EU (783; 21%), Asia (959; 25%) and Central America (760; 20%), median time from RA diagnosis was 5 years, 2938 (78%) and 1754 (47%) were on concomitant MTX or corticosteroids (CS; mean dose 6.2 mg/day), respectively. HZ was reported in 323 (9%) pts over 9892 PYO, with median BARI exposure of 1115 days. Of these pts, 12 (4%) had a history of HZ, and 256 (79%) and 168 (52%) were on concomitant MTX and CS, respectively. The median time to first HZ event was 538 days and the overall IR of HZ was 3.3/100 PYO, which did not increase significantly over time (Fig 1). Twenty-six (8%) cases were multidermatomal, and no visceral disease was reported. Eight (2%) pts showed involvement of the ophthalmic division of the Vth cranial nerve and 9 (3%) experienced recurrent HZ during observation. Only 11 HZ pts (4%) had received prior HZ vaccination. Multivariate analyses showed that older age (hazard ratio [HR] 1.30, 95% confidence interval [CI] 1.17, 1.43) and geographical region (Asia, especially Japan, Taiwan and South Korea; HR 1.82, 95% CI 1.28, 2.58; Fig 2) were associated with a higher risk of HZ.
Conclusion: HZ incidence in BARI-treated RA pts did not increase over time and the majority of HZ events were monodermatomal and uncomplicated. Pts who were older and those from Asia were at increased risk of a HZ event.

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[1] Smitten AL, et al. Arthritis Rheum 2007;57:1431–1438. 2. Smolen JS, et al. J Rheumatol 2019;46:7–18.

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