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RAPID RESPONSE TO BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE AND AT LEAST ONE BIOLOGIC DMARD: A CLINICAL AND POWER DOPPLER ULTRASOUND STUDY

C. Baldi¹, P. Falsetti¹, E. Conticini¹, S. G. Khayyat¹, M. Bardelli¹, S. Gentileschi¹, L. Cantarini¹, B. Frediani¹. ¹Rheumatology Unit, University of Siena, Siena, Italy

Background: Baricitinib, an oral Janus kinase (JAK) 1-2 inhibitor, is currently used among biologic DMARDs (bDMARDs) after the failure of methotrexate (MTX) in rheumatoid arthritis (RA). Power Doppler ultrasound (PDUS) is a promising, non-invasive imaging method to assess synovitis in RA: results from numerous studies suggest that it provides additional information to clinical and conventional radiographic examinations.

Objectives: The main objective of our study was to evaluate short-term efficacy of Baricitinib in reducing synovitis, using the composite semi quantitative scale (0–3 grades) PDUS synovitis score, developed by the Outcome Measures in Rheumatology–European League Against Rheumatism (OMERACT–EULAR)–Ultrasound Task Force. Moreover both synovial hyperplasia and intrasynovial power Doppler (PD) signal were also scored as single components/parameters on 0–3 scales. Secondary objective was to assess the concordance between patient reported outcomes (PROs), markers of inflammation, physical examination and US.

Methods: We enrolled 30 patients fulfilling 2010 ACR and EULAR criteria for RA. All patients had failed at least one anti-TNF. Each patient was prescribed Baricitinib 4mg/daily at T0, in addition to MTX and/or oral steroids at a dosage ≤ 7.5 mg/day of Prednisone or equivalent, at T: All patients were evaluated at baseline (T0) and then after one month (T1), 3 months (T2) and 6 months (T3) of treatment. Swollen and tender joints (out of 28) were evaluated and recorded, as well as patient (PGA) and physician global assessment (PhGA) and pain, expressed in a visual analog scale (VAS). Disease activity was evaluated at each visit using DAS28 (Disease activity score 28), CDAI (Clinical disease activity index) and SDAI (Simplified disease activity index), accompanied by a complete blood count, Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) collection. Statistical analysis was performed using GraphPad version 9.0.0. PDUS examination, was carried out by two rheumatologists (PF and CB) blinded to clinical conditions of the patients, using an Esaote Mylab Twice (Genoa, Italy), equipped with a high-frequency (6–18 MHz) linear probe. With standardised Doppler parameters (pulse repetition frequency between 500–750 Hz; Doppler frequency between 7–11.1 MHz). PDUS was performed at each visit bilaterally for 22 joint sites [MCPs 1–5, proximal interphalangeal joints (PIPs) 1–5, wrist, elbow, glenohumeral, knee, tibiotaral, talonavicular and calcaneocuboidal and metatarsophalangeal joints (MTPs) 1–5] for a total of 44 joints for each patient.

Results: We observed a reduction of VAS pain (T0 vs. T6 $p < 0.0001$) PDUS composite score (T0 vs. T6 $p < 0.0001$), Power Doppler (T0 vs. T6 $p < 0.0001$) synovial hyperplasia (T0 vs. T6 $p = 0.0002$), CRP (T0 vs. T6 $p < 0.0001$) and ESR (T0 vs. T6 $p < 0.0001$) was observed in our patients. Accordingly, DAS-28, CDAI and SDAI displayed a significant reduction too (DAS-28: T0 vs. T6 $p < 0.0001$; CDAI: T0 vs. T6 $p < 0.0001$; SDAI: T0 vs. T6 $p = 0.0003$).

Conclusion: We investigated the efficacy of Baricitinib in real life, evaluating both from a clinimetric and ultrasound point of view. Baricitinib demonstrated a significant parallel and fast improvement in VAS, PDUS and CRP was found at follow up assessment as early as one month of therapy. In conclusion, these results demonstrated the short term efficacy of Baricitinib 4mg for up to 6 months and providing a prompt improvement of PROs within the first weeks of treatment.

Figure 1. The difference between the means of PD and of the VAS pain over time (T0, T1, T3 and T6). Power Doppler (T0 vs. T6** $p < 0.0001$), VAS: (T0 vs. T1 * $p < 0.0098$; T0 vs. T3 **** $p < 0.0001$; T0 vs. T6 **** $p < 0.0001$)

Disclosure of Interests: None declared

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PREDICTORS OF TOXICITY WITH HYDROXYCHLOROQUINE AND CHLOROQUINE USE: A SYSTEMATIC REVIEW

N. Citeroni¹, S. Rampes¹, P. Kotecha¹, J. Schoones², E. Nikiphorou^{3,4}, J. Galloway^{3,4}. ¹King's College London, GKT School of Medical Education, Faculty of Life Sciences & Medicine, London, United Kingdom; ²Leiden University Medical Center, Walaeus Library, Leiden and the Hague, Netherlands; ³King's College London, Centre for Rheumatic Diseases, London, United Kingdom; ⁴King's College Hospital, Rheumatology Department, London, United Kingdom

Background: Hydroxychloroquine (HCQ) has attracted much attention especially during the COVID-19 pandemic. HCQ and closely related chloroquine (CQ) have known ocular and cardiac toxicity. However, although screening guidance now exists from the Royal College of Ophthalmologists for the former (RCOphth)¹, little is known regarding predictors of both forms of toxicity.

Objectives: To systematically explore the literature on predictors of toxicity limited to cardiac and ocular toxicity.

Methods: A detailed search of the following databases was conducted: PubMed, Medline, Embase, Web of Science, The Cochrane library, EMCare and Academic Search Premier. Studies addressing predictors of HCQ toxicity with relevant search terms used were included. Exclusion criteria were: non-English articles, pre-clinical and paediatric studies. Three authors (SR, NC, PK) independently screened titles and abstracts for inclusion, ensuring each article was screened twice. Disagreement over inclusion was adjudicated by senior reviewers (EN, JG). Data extraction (SR, NC, PK) focused on predictors of toxicity.

Results: The search strategy retrieved 3103 studies. 147 studies were included for data extraction, of which 92 were eventually excluded due to: not identifying predictors (n=17), reviews (n=19), not ocular or cardiovascular toxicity (n=18), case reports (n=3), paediatrics (n=1), screening articles that focused on detecting retinopathy (n=30), article unobtainable at time of abstract submission (n=4), leaving 55 studies for full review.

Studies addressing cardiac toxicity (n=16) included: cohort, retrospective observational, a comparative pharmacovigilance, systematic monitoring protocol and a randomised control trial (RCT). The majority of these involved high-dose (>5mg/kg/day) use for acute COVID-19 infection. The main significant predictors identified were: Hydroxychloroquine (HCQ) use in combination with azithromycin (6/7 studies), cumulative dose (2 studies), pre-existing cardiovascular morbidity (2/3 studies) and prolonged baseline QTc (2 studies). Individual associations were also identified in the following: longer treatment duration, daily dosage, increased age, male gender, severe COVID-19 infection, abnormal liver function tests (LFTs) and concurrent use of loop-diuretics.

Regarding predictors of ocular toxicity (n=39), only one study was a RCT. The remainder were observational studies: case-control, cohort, retrospective chart reviews and letters to the editor which included original patient data.

Several predictors of retinopathy and maculopathy were examined in two or more studies and included: duration of use (16/18 studies), daily dosage (7/13 studies), cumulative dose (11/14 studies), increased age (10/11 studies), body weight or BMI (3/5 studies), renal impairment (5 studies), HCQ blood levels (2 studies),