Rheumatoid arthritis - non biologic treatment and small molecules - PART 1

POS0086 ANALYSIS OF DISEASE ACTIVITY MEASURES IN THE CONTEXT OF A METHOTREXATE WITHDRAWAL STUDY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB 11 MG ONCE DAILY + METHOTREXATE: POST HOC ANALYSIS OF DATA FROM ORAL SHIFT

R. Fleischmann1, B. Harauzi2, M. H. Buch3,4, D. Gold5, G. Sawyer6, H. Shi7, A. Diehl7, K. Lee5. 1Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Department of Medicine, Dallas, TX, United States of America; 2Institut de Rhumatologie de Montréal, Montreal, QC, Canada; 3School of Biological Sciences, Faculty of Biology, Medicine & Health, University of Manchester Centre for Musculoskeletal Research, Manchester, United Kingdom; 4NHRI Manchester Biomedical Research Centre, Manchester, United Kingdom; 5Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America; 6Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America

Background: The Phase 3xiv study ORAL Shift demonstrated sustained efficacy and safety of tofacitinib modified-release (MR) 11 mg once daily (QD) following methotrexate (MTX) withdrawal that was not inferior to continued tofacitinib + MTX use (per DAS28-4[ESR]), in patients (pts) with rheumatoid arthritis (RA) who achieved CDAI-defined low disease activity (LDA) with tofacitinib + MTX at Week (W)24.1

Objectives: To assess the performance of alternative disease activity measures at W24 (randomisation) and W48 (study endpoint) in ORAL Shift.

Methods: ORAL Shift (NCT02831855) enrolled pts aged ≥18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label tofacitinib MR 11 mg QD + MTX for 24 weeks. Achievement of CDAI LDA (≤10) at W24 was set as the criteria for entry to the 24-week double-blind MTX withdrawal phase, with pts randomised 1:1 to receive tofacitinib MR 11 mg QD + placebo (PBO) (ie blinded MTX withdrawal) or continue tofacitinib + MTX. In this post hoc analysis, efficacy analyses were performed in 8 subgroups defined by achievement of various disease activity criterion at W24: DAS28-4[ESR] remission (≤2.6) or LDA (≤3.2); DAS28-4[CRP] <2.6 or ≤3.2; RAPID3 remission (≤3) or LDA (≤8); CDAI remission (≤28); and SDAI remission (≤33). For each subgroup, the proportion of pts who achieved the corresponding disease activity criterion at W48 was calculated, with a 95% confidence interval (CI) estimated using the normal approximation to the binomial distribution. The change (Δ) from W24 to W48 in least squares mean (LS mean) ΔDAS28-4[ESR] and ΔDAS28-4[CRP] was also calculated in each subgroup, with a 95% CI for the difference between treatment groups estimated using a mixed model with repeated measures. Nominal p values were calculated and are presented with no formal statistical hypothesis testing formulated.

Results: Overall, 694 pts entered the open-label phase of ORAL Shift, and 530 were randomised and received treatment in the double-blind phase; 264 and 266 pts received tofacitinib + PBO and tofacitinib + MTX, respectively (Figure 1a). Considering those pts who were randomised and treated, the proportion of pts achieving each disease activity criterion at W24 varied, but was similar between treatment groups in all subgroups. The majority of pts in both treatment groups also achieved each disease activity criterion at W24, with or without confirmed MTX. Differences between treatment groups in LS mean ΔDAS28-4[ESR] from W24 to W48, as defined by achievement of LDA or remission with a variety of disease activity measures, were less than a change of 1.2, which is considered to be the threshold for a minimal clinically important improvement.2

References:


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POS0087 LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB OR ADAEBALUMIN IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 3 YEARS FROM THE SELECT-COMPARE STUDY

R. Fleischmann1, E. Myers2, L. Bessette3, C. Peterfy4, P. Durez5, Y. Tanaka6, J. Swierko7, N. Khan8, X. Bu9, Y. Li1, H. H. Song1. 1Univ of Texas Southwestern Med Center, Metropolis Clinical Research Center, Dallas, United States of America; 2Organizacion Medica de Investigacion, Rheumatology, Buenos Aires; Argentina; 3Laval University, Rheumatology, Quebec, Canada; 4Spira Sciences Inc, Boca Raton, United States of America; 5Institut de Recherche Expérimentale et Clinique, UCL Saint-Luc, Pôle de Recherche en Rhumatologie, Brussels, Belgium; 6University of Occupational and Environmental Health, The First Department of Internal Medicine, Kitakyushu, Japan; 7Wroclaw Medical University, Department of Rheumatology and Internal Medicine, Wrocław, Poland; 8AbbVie, Immunology, North Chicago, United States of America

Background: In the SELECT-COMPARE study, the Janus kinase inhibitor, upadacitinib (UPA), demonstrated significant improvements in the signs and symptoms of rheumatoid arthritis (RA) when administered at 15 mg once daily (QD) on background methotrexate (MTX) compared to adalimumab (ADA) plus MTX at Week 12 that were maintained through 72 weeks in patients with prior inadequate response to MTX.1

Objectives: To assess the long-term safety and efficacy of UPA vs ADA over 3 years in the ongoing long-term extension (LTE).

Methods: Patients receiving background MTX were randomized 2:2:1 to UPA 15 mg QD, placebo (PBO), or ADA 40 mg every other week. Between Week 14-26, rescue was mandated for either lack of response (<20% improvement in tender or swollen joint counts: Weeks 14, 18, 22) or failure to achieve a targeted disease activity criterion at Week 12 that were maintained through 72 weeks in patients with prior inadequate response to MTX.1

Results: In total, 651, 655, and 327 patients were randomized at baseline to receive UPA, PBO, and ADA, respectively. Between Weeks 14-26, 252 (39%) patients were rescued from UPA to ADA, 159 (49%) were rescued from ADA to UPA, and all PBO patients were switched to UPA by Week 26.2 A higher proportion of patients randomized to UPA completed 3 years without rescue compared to those randomized to ADA (47% vs 36%, respectively). UPA was generally well-tolerated as assessed by the rates of TEAEs, including serious AEs, AEs leading to discontinuation of study drug, and AESIs, including serious and opportunistic infections, malignancies, adjudicated major adverse cardiac events or venous thromboembolism; Figure 1). Consistent with previous analyses, the event rates of AESIs were generally comparable between the UPA and...

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