OP0130

ABATACEPT IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS: RESULTS FROM THE ARTHRITIS PREVENTION IN THE PRE-CLINICAL PHASE OF RA WITH ABATACEPT (APIPPRA) TRIAL

Keywords: Randomized control trial

A. Cope[1,2], M. Jasenecova[1], J. Vasconcelos[3], A. Filer[4], K. Raza[4,5], S. Qureshi[1], M. A. D'agostino[6], I. Mcinnes[7], J. Isaacs[8], A. Pratt[8], B. Fisher[4], C. D. Buckley[9], P. Emery[10,11], P. Ho[12], M. H. Buch[12], C. Ciurtin[13], T. Huizinga[14], D. Van Schaardenburg[15], C. Murphy[16], T. Prevost[3]. [1]*King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; [2]*Guy's and St Thomas' NHS Foundation Trust, Department of Rheumatology, London, United Kingdom*; [3]*King's College London, Nightingale-Saunders Clinical Trials & Epidemiology Unit, London, United Kingdom*; [4]*University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom*; [5]*Sandwell and West Birmingham NHS Trust, Department of Rheumatology, Birmingham, United Kingdom*; [6]*Catholic University of the Sacred Heart, Division of Rheumatology, Rome, Italy*; [7]*University of Glasgow, School of Infection and Immunity, Glasgow, United Kingdom*; [8]*Newcastle University, Translational & Clinical Research Institute, Newcastle, United Kingdom*; [9]*University of Oxford, Kennedy Institute of Rheumatology, Oxford, United Kingdom*; [10]*University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [11]*Leeds NIHR Biomedical Research Centre, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [12]*University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [13]*University College London, Centre for Rheumatology Research, London, United Kingdom*; [14]*Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; [15]*Amsterdam University Medical Centers, Reade, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*; [16]*King's College London, King's Clinical Trials Unit, London, United Kingdom*

Background: While genetic and epidemiological factors have been used traditionally to evaluate the risk of developing rheumatoid arthritis (RA), the definition of higher risk states has been refined in more recent years through inclusion of serum autoantibodies and symptom complexes, such as inflammatory joint pain. Data from at risk cohorts have reported rates of progression to RA in excess of 50% over 24 months. These combined features have provided a framework for the design of interception studies, aimed at delaying or preventing RA.

Objectives: We evaluated the feasibility, efficacy and acceptability of T-cell co-stimulation modulation with abatacept in individuals at risk of developing RA in the Arthritis Prevention In the Pre-clinical Phase of RA with Abatacept (APIPPRA) study.

Methods: APIPPRA is a Phase IIB randomised, double blind, placebo-controlled trial recruiting $ACPA^{+}RF^{+}$ or $ACPA^{hi}$ (≥3 x ULN) RF^{-} individuals with arthralgia. Consenting participants were randomised, stratified by gender, smoking status and country, to receive 52 weekly subcutaneous injections of placebo or 125mg abatacept, and followed up for a further 52 weeks after stopping treatment. Exclusion criteria included previous episodes of clinical synovitis, prior corticosteroids or DMARDs. The primary endpoint was the time to development of either clinical synovitis in ≥3 joints, or RA according to ACR/EULAR 2010 criteria, whichever was met first, where joint involvement required swelling. Joint synovitis was confirmed by ultrasonography. The study was powered to detect a 50% reduction in progression in those receiving abatacept. Secondary endpoints included multiple disease activity assessments, the time to commencing DMARDs and/or corticosteroids, X-ray and ultrasound scores, as well as safety data. The main ITT analysis was repeated in a per-protocol population of participants who did not take forbidden medication, and who, in the first year or up to a primary event, had 90% adherence to treatment.

Results: Between December 2014 and January 2019, 280 individuals were evaluated for eligibility across 31 study sites, 28 in the UK and 3 in the Netherlands. Two hundred and thirteen were randomised, 103 to placebo and 110 to abatacept. Mean age was 49 and 77% were female. Ninety-three percent of individuals were $ACPA^{hi}$. Ultrasonography at baseline suggested modest levels of active sub-clinical synovitis (73% of participants with power Doppler score of 0). In total, there were 65 primary outcome events. After stopping treatment at 52 weeks there were 30 events (29%) in the placebo arm and 7 (6%) in the abatacept arm. By the end of the study there were 38 (37%) and 27 (25%) events, respectively, resulting in differences in mean arthritis-free survival time between arms of 99.2 days (95% CI 37.5 – 160.9; *p*-value=0.002), in favour of abatacept. The respective log-rank test for difference in the survival distribution was *p*=0.044, reflecting a large effect in the first year and convergence over the second year (see Figure 1). The per protocol analysis showed similar results. The cumulative proportion of arthritis-free participants at 52 weeks was 0.692 (SE 0.047) in the placebo arm and 0.928 (SE 0.026) for the abatacept arm, and 0.585 (SE 0.054) for placebo and 0.704 (SE 0.048) for abatacept at 104 weeks. *Post hoc* analysis revealed that individuals with an extended autoantibody profile at baseline were more likely to remain arthritis-free following abatacept therapy. Those treated with abatacept had lower tender joint counts and pain scores during the treatment period, when compared to placebo. There were 4 serious adverse events in the abatacept group and 10 in the placebo group, including two deaths, one in each arm, none deemed attributable to study drug.

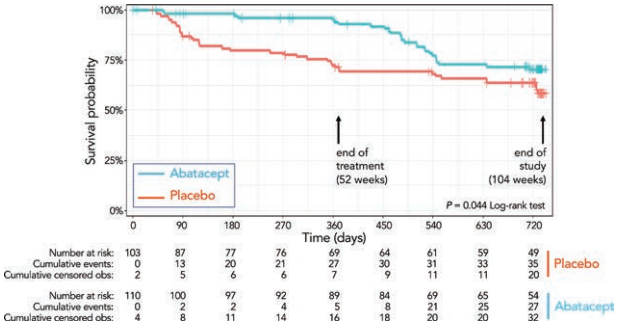

Figure 1.

Conclusion: Therapeutic intervention during the RA at risk phase is feasible, with acceptable safety profiles. T cell co-stimulation modulation with abatacept for 52 weeks showed a reduction in the development of RA over two years. There were no new safety signals.

Acknowledgements: The APIPPRA trial is an Investigator Sponsored Research (ISR) study funded by Bristol Myers Squibb, and jointly sponsored by Guy's and St Thomas' NHS Foundation NHS Trust and King's College London in the UK and Leiden University Medical Center in the Netherlands. Bristol Myers Squibb played no role in data acquisition or analysis.

Disclosure of Interests: Andrew Cope Speakers bureau: BMS, Abbvie, Galapagos, Consultant of: BMS, GSK, Abbvie, Grant/research support from: BMS, Janssen, UCB, Marianna Jasenecova: None declared, Joana Vasconcelos: None declared, Andrew Filer Grant/research support from: Roche, UCB, Nascient, Mestag, GSK, Janssen, Karim Raza Grant/research support from: BMS, Sumera Qureshi: None declared, Maria-Antonietta D'Agostino: None declared, Iain McInnes Consultant of: BMS, Grant/research support from: BMS, John Isaacs Speakers bureau: AbbVie, BMS, Gilead, Roche, Consultant of: AbbVie, BMS, Gilead, Roche, Grant/research support from: GSK, Janssen and Pfizer, Arthur Pratt Consultant of: Inflection Biosciences, Grant/research support from: GSK, Pfizer, Galapagos, Benjamin Fisher Consultant of: Novartis, Roche, BMS, Galapagos, Servier, UCB, Janssen, Grant/research support from: Janssen, Galapagos, Servier, Celgene, Christopher D Buckley: None declared, Paul Emery Consultant of: BMS, Grant/research support from: BMS, Pauline Ho: None declared, Maya H Buch: None declared, Coziana Ciurtin: None declared, Thomas Huizinga Speakers bureau: BMS, Consultant of: BMS, Grant/research support from: BMS, Dirkjan van Schaardenburg Speakers bureau: BMS, Caroline Murphy: None declared, Toby Prevost: None declared.

DOI: 10.1136/annrheumdis-2023-eular.1751

OP0131

DISEASE ACTIVITY-GUIDED DOSE OPTIMIZATION INCLUDING DISCONTINUATION OF TNF-INHIBITORS IN RHEUMATOID ARTHRITIS IS EFFECTIVE FOR UP TO 10 YEARS: RESULTS OF THE DRESS STUDY

Keywords: bDMARD, Rheumatoid arthritis, Tapering

C. Van der Togt[1], N. Den Broeder[1], A. Van der Maas[1], A. Den Broeder[1,2], N. Van Herwaarden[1,3]. [1]*Sint Maartenskliniek, Rheumatology, Ubbergen, Netherlands*; [2]*Radboud University Medical Center, Rheumatology, Nijmegen, Netherlands*; [3]*Radboud University Medical Center, Pharmacology-toxicology, Nijmegen, Netherlands*

Background: Tumor necrosis factor inhibitors (TNFi) are effective in rheumatoid arthritis (RA) but have their drawbacks such as the need for self-injection, infections and costs. To reduce these disadvantages, disease activity-guided dose optimization (DAGDO) has shown to be an effective and safe strategy.[1] During DAGDO, a stepwise dose reduction of the TNFi is performed if allowed by the disease activity. In the Dose Reduction Strategy of Subcutaneous TNFi (DRESS) study, effectiveness and safety of DAGDO has been shown in RA patients for up to three years.[2, 3] However, long term outcomes of DAGDO are scarce, and it is debated whether a discontinuation attempt should be included.

Objectives: To assess 10-year effectiveness of DAGDO of TNFi in the DRESS cohort, specifically 1) disease activity over time, 2) biological and targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) dose over time, 3)