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WEDNESDAY, 12 JUNE 2019

18:15:00 – 19:45:00

Personalised medicine in rheumatic disease

SP0034 RA-MAP. PATIENT STRATIFICATION IN RA

John Isaacs. Newcastle University, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom

Background: When we assess rheumatoid arthritis in the clinic we quantify inflammation. Apart from measuring auto-antibodies we do not assess the immune system.

Objectives: The MRC/ABPI RA-MAP study was an academia-industry consortium designed to characterise the immune dysregulation that presents clinically as RA¹. Key questions were:

- o Are there baseline immune markers of prognosis/therapeutic response?
- o What is the molecular signature of the disease state (is there an immune correlate of inflammation)?
- o Can 'RA' be defined in terms of immune dysregulation and are there distinct subtypes?

Methods: RA-MAP was a systems immunology analysis of 275 patients with seropositive, treatment-naïve early RA (the TACERA cohort). Patients were assessed at baseline and every 3 months for up to 18 months. At each visit, clinical samples were collected for transcriptomic (blood), proteomic (blood) and metabolomic (blood and urine) analyses. Peripheral blood mononuclear cells were characterised by flow cytometry. Clinical and demographic information was collected at each visit. Primary analyses addressed the key questions by seeking associations between immune parameters and disease activity or disease state.

Results: Latent class analysis of clinical data revealed three main disease trajectories². Transcriptomic and systems approaches highlighted at least two subtypes of seropositive RA. Proteomic analyses also supported multiple RA subtypes. Metabolomic analyses revealed prognostic baseline signatures. Flow cytometry revealed a reduction in peripheral blood mononuclear cell complexity as disease became less active. Combinatorial analyses of different datasets is currently underway.

Conclusion: RA-MAP has provided important insights into the immunological and molecular heterogeneity of RA. Our findings require replication and validation, and some analyses are ongoing. RA is the consequence of dysregulated immunity characterized by distinct molecular 'endotypes'.

REFERENCES:

- [1] Cope AP, et al. The RA-MAP Consortium: a working model for academia-industry collaboration. *Nat Rev Rheumatol* 2018;14:53-60. doi: 10.1038/nrrheum.2017.200
- [2] Tom BDM, et al. Novel methodology to discern predictors of remission and patterns of disease activity over time using rheumatoid arthritis clinical trials data. *RMD Open* 2018;4:e000721. doi:10.1136/rmdopen-2018-000721

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SP0035 PRECISION MEDICINE IN PSA

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Background: Biological DMARDs targeting particular molecules relevant to pathological processes have revolutionized the treatment of rheumatoid arthritis (RA) and clinical remission is now realistic targets. However, several issues to be addressed still remain. First, less than half of patients who are treated with methotrexate and biological DMARDs achieved remission defined by stringent composite measures. Second, from multiple biological DMARDs, how to select the most appropriate treatment in each patient remain unclear. Third, how to expand the treatment strategies learned from RA to other rheumatic and/or systemic autoimmune diseases are still under investigations.

Objectives: Psoriatic arthritis (PsA) is a typical complication of psoriasis that causes irreversible destruction and dysfunction of joints and/or the spine and

appropriate and timely intervention is prerequisite to inhibit progress in the damages. Various cytokines including IL-12, IL-23, IL-17 and TNF play important roles in the pathogenesis of PsA. Therefore, biological DMARDs targeting these key effector cytokines are currently available and actually effective in supporting the resolution of enthesitis and subsequent arthritis as well as damages of spine/joint in PsA.

Methods: We have compared efficacies of biological DMARDs in PsA patients who were treated according to 2015 EULAR recommendations and whose biological DMARDs were strategically selected based on peripheral blood lymphocyte phenotyping using 8-colour flow cytometry with specific focus on helper T cell subsets.

Results: Patients with PsA were divided to 4 groups by the dominance of Th1- and Th17-phenotypes and biological DMARDs were stratified in each subgroup: an anti-p40 antibody to the activated Th1 cell-predominant patients, anti-IL-17 antibodies to the activated Th17 cell-predominant, IL-17 inhibitors or TNF inhibitors to the Th1/Th17-high, and TNF inhibitors to the Th1/Th17-low patients. Significant improvement of simplified disease activity index (SDAI) and psoriasis area and severity index by both the standard treatment and the strategic selection of biological DMARDs after the 6-month treatments. It is noteworthy SDAI values were improved in the vast majority of patients in the strategic treatment group, whereas the values were sustained in some patients despite standard biological DMARDs.

Conclusion: Although accumulation of evidence and development of new markers are expected, the obtained results indicate potential for precision medicine via the strategic selection of different biological DMARDs for PsA based on the phenotypic differences in peripheral helper T cells.

REFERENCES:

- [1] Miyagawa I, Nakayamada S, Nakano K, Kubo S, Iwata S, Miyazaki Y, Yoshikawa M, Yoshinari H, Tanaka Y. Precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in psoriatic arthritis. *Rheumatology* (2019) 58: 336-344.
- [2] Tanaka Y. Psoriatic arthritis in Japan: difference in clinical features and approach to precision medicine. *Clin Exp Rheumatol* (2016) 34, 49-52.

Disclosure of Interests: Yoshiya Tanaka Grant/research support from: Abbvie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Ono, Taisho-Toyama, Takeda, Speakers bureau: Abbvie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-SmithKline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics

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SP0036 MASTERPLANS – TAILORING SLE FOR THERAPY

Ian N. Bruce. University of Manchester, United Kingdom

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease which is highly heterogeneous in its clinical manifestations and also in its response to specific therapies. Across a number of trials of novel agents, overall response rates are approximately 40-60% and in the past almost 60 years only one drug (belimumab) has been licensed for use in SLE. Current therapy is therefore based on a 'trial and error' approach frequently involving glucocorticoid co-therapy. Delayed and poor control of inflammation results in organ damage, cardiovascular disease and glucocorticoid toxicity. We established a consortium of academia and industry partners (MAXimizing SLE Therapeutic Potential by Application of Novel and Stratified approaches (MASTERPLANS) with the aim of identifying key endotypes associated with response and low disease activity on particular therapies.

Objectives: Our consortium is addressing the hypothesis that strata exist within SLE populations that will enable more targeted use of existing and novel therapeutic agents and improve response rates. Specifically, B-cell related biomarkers including dynamics and function predict responses to mycophenolate mofetil (MMF) and B-cell targeted biologics and interferon signature/pathway dynamics identifies patients with poorer responses to these agents.

Methods: Our approach will firstly be to re-analyse data already available from large studies and trials to identify key predictive factors of response. Also, using data from a large UK cohort, the BiLAG-Biologics Register, we will assess clinical factors and biomarkers that predict response and low disease activity. Combining results from these studies with that gained from previous studies will enhance our ability to identify endotypes of response.

Conclusion: Identifying biomarkers of response will allow better selection of therapy for individual patients. Using the right drug at the right time will improve control of inflammation for patients with SLE and contribute to improving long-term outcomes.

Disclosure of Interests: Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline,

ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma

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SP0037 USING GENETICS IN PERSONALISED MEDICINE IN RHEUMATIC DISEASES

Anne Barton. University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom

Background: For all treatments available for rheumatoid arthritis (RA), none are effective for all patients. For many drugs, patients are given 3-6 months of treatment before a decision is made regarding efficacy and, for those in whom the treatment does not work, that can be a period of on-going disease activity, exposure to the risk of side effects and possible accumulation of joint damage, all of which impact quality of life. Stratified medicine approaches aim to better target treatments to those most likely to respond. However, currently, CRP/ESR are the only biological markers (biomarkers) routinely used to inform whether therapy is required and RF/ACPA status are often considered.

Objectives: To update in progress of using genomic approaches to inform treatment selection in rheumatoid arthritis

Methods: National and international precision/stratified medicine programmes are investigating whether genetic and epigenetic biomarkers could help in the selection of therapies and progress will be reviewed.

Results: Recent studies have developed new outcome measures to assess treatment efficacy for controlling synovitis, confirming previous findings from genetic studies of heritability. Issues around the best tissue to sample, the predictive ability of a test and confounding factors including adherence will be considered and emerging biomarkers reviewed.

Conclusion: Matching the right treatments to the right patients is the goal of personalised medicine and potential biomarkers are starting to emerge. However, caution is required as none have so far been proven to be clinically useful or cost-effective.

REFERENCE:

- [1] Hensor, et al. Rheumatology 2019; Plat et al, Arthritis and Rheumatol 2019.

Disclosure of Interests: None declared

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WEDNESDAY, 12 JUNE 2019

18:15:00 – 19:45:00

The riddle of adherence

SP0038 FACTORS IMPORTANT FOR MEDICAL ADHERENCE

Bart van den Bemt. Sint Maartensliniek, Netherlands

Factors important for medical adherence in rheumatic diseases Disease-modifying antirheumatic drugs (DMARDs) are the cornerstone for the treatment of inflammatory arthritis and fundamental to prevent radiologic progression in patients with rheumatoid/psoriatic arthritis. However, the full benefit of DMARDs can only be achieved if patients follow prescribed treatment regimens. Adherence, or the extent to which patients take medications as prescribed, is however low in chronic medical conditions: approximately 50% of all people with chronic medical conditions do not adhere to their prescribed medication regimens [1,2]. Previous research in patients with rheumatic diseases vary from 30% to 107%, depending on the used measurement method [7].

Thus, improving adherence to DMARDs could dramatically improve the efficacy of drug therapy in rheumatic diseases and reduce costs. However, so far, interventions designed to improve medication adherence are only partly effective in changing medication-taking behaviour [2-5].

To be able to improve adherence, factors should be known that are associated with medication adherence in RA. This will help us to target non-adherent patients and design interventions to improve adherence. Although several studies have examined factors associated with adherence to treatment with DMARDs, hardly any variable was found to be consistently and strongly related to adherence. [6-7]. Despite this, there is evidence that especially patient's need to take medication, prior DMARD use, patient's self-efficacy and information delivered to the patient might be associated with medication adherence.

Overall, two types of non-adherent behaviour are commonly observed: unintentional (due to forgetfulness, regimen complexity or physical problems) and intentional (when the patient decides not to take the treatment as instructed). In case of

intentional non-adherence, the decision to take medication is based on a cost benefit analysis weighing the costs/risks of the treatment against the perceived benefits. This implicates that health care professionals should individually assess patient's (un)intentional barriers to take medication and target medication adherence interventions on patient's individual barriers. Thus, besides tackling (unintentional) practical barriers, such as forgetfulness (with for example reminder services), clinicians should also be sensitive to patient's personal beliefs that might impact medication adherence, and should discuss with their patient any concerns that they raise about prescribed medications. This lecture will give insight in the latest insights in the research of factors important for medication adherence and their practical consequences for adherence improving interventions in clinical practice.

REFERENCE:

- [1] Sabate E, ed. Adherence to long-term therapies: evidence for action. Geneva, World Health Organization, 2003.
- [2] Nieuwlaar R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B, Iserman E, Mustafa RA, Jedraszewski D, Cotoi C, Haynes RB. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev.* 2014; (11)
- [3] Galo JS, Mehat P, Rai SK, Avina-zubieta A, Vera MA De. What are the effects of medication adherence interventions in rheumatic diseases: a systematic review. *Ann rheum Dis.* 2016;75: 667–673.
- [4] Demonceau J, Ruppar T, Kristanto P, Hughes DA, Farger E, Kardas P, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. *Drugs.* 2013;73: 545–562.
- [5] Lavielle M, Puyraimond-zemmour D, Romand X, Gossec L, Senbel E, Pouplin S, et al. Methods to improve medication adherence in patients with chronic inflammatory rheumatic diseases: a systematic literature review. *RMD Open.* 2018;4: 1–8.
- [6] Van den Bemt BJ, Zwicker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. *Expert Rev Clin Immunol.* 2012;8(4):337-51.
- [7] Pasma A, van't Spijker A, Hazes JM, Busschbach JJ, Luime JJ. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. *Semin Arthritis Rheum.* 2013 Aug;43 (1):18-28. doi: 10.1016/j.semarthrit.2012.12.001. Epub 2013 Jan 24.

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THURSDAY, 13 JUNE 2019

10:15:00 – 11:45:00

Advances in understanding and treating of SLE

SP0039 WIN: DE-CONVOLUTING THE COMPLEXITIES OF SLE – RECENT INSIGHTS INTO THE PATHOGENESIS

Mary K. Crow. Hospital for Special Surgery, Weill Cornell Medical College, Mary Kirkland Center for Lupus Research, United States of America

Background: SLE remains one of the most complex diseases in medicine, with protean alterations in immune system function contributing to autoimmunity, tissue inflammation and damage, and diverse clinical manifestations. While considerable advances in understanding the molecular pathways and mediators involved in SLE have led to identification of rational therapeutic targets, a full understanding of the upstream etiologic drivers of the disease and how genetic risk and environmental stimuli shape the evolution of the disease and its clinical heterogeneity requires continued investigation.

Objectives: To review recent literature relevant to the etiology, pathogenesis and heterogeneity of SLE.

Methods: Review and synthesis of recent literature.

Results: Recent advances in characterizing the mechanisms of regulation and degradation of endogenous nucleic acids, particularly insights derived from disorders based on a variety of single gene mutations that result in production of type I interferon, suggest potential drivers of type I interferon production in SLE. The functional alterations in many aspects of T and B cell function in patients with SLE, some attributable to type I interferon, continue to be identified. Potential contributions of the microbiome expand our view of candidate disease-enhancing factors. Interest in defining patients at risk for evolving from pre-clinical to clinical disease