use of different calibrators and by the fact that drug tolerance differs among assays ranging from extreme drug sensitive over various forms of drug tolerant to drug resistant anti-drug antibody asssays. The clinical relevance of the different type of anti-drug antibody assays remains to be proven.
Combining therapeutic drug concentrations and anti-drug antibody concentrations with relevant patient, disease and drug information will lead to optimal dosing of patients aiming at optimal clinical, biochemical and endoscopic outcomes.
Disclosure of Interest: A. Gils Grant/research support from: IIR grants from pfizer, Speakers bureau: speakers fee by Pfizer, MSD, Abbvie, Takeda, JnJ
DOI: 10.1136/annrheumdis-2017-eular.7210

SP0083 AS A RHEUMATOLOGIST, DOES IT HAVE ANY CONSEQUENCE IN MY DAILY PRACTICE?

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It is nearly inevitable that when we administer foreign (even humanised) proteins intravenously or subcutaneously to a person, that said person will develop antibodies to that (foreign) protein. This happens to most of our patients when we administer biologicals; depending on the sensitivity of our methods, we can measure these anti-bodies easily or not at all. These antibodies start becoming a problem when they are actually binding the administered biological, thus making the active drug less available for its targeted function. We can evaluate this by measuring the actual drug-level, so called trough level. Numerous reports have been published, showing that there is indeed a negative correlation between e.g. anti-tumor necrosis factor (TNF) drug antibodies and the efficacy of anti TNF in the treatment of RA. It has also been shown that adding methotrexate (MTX) to the anti-TNF treatment improves its efficacy and reduces the level of anti-drug antibodies. Probably only 10 mg MTX weekly would be enough to obtain this effect.
So what do I do as a clinician when I observe that a patient, who originally did very well, loses response to her biological? Do I measure possible anti-drug antibodies? No, the consequences are zero: When the patient is not responding to the given drug anymore, I need to adapt the treatment; the drug she is using is not effective anymore, so we should change. Would the presence of anti-drug antibodies influence my decision? No, there is no cross-reactivity to other biologicals (even from the same class of action), except to its biosimilar (underscoring that it is a real biosimilar!). In case there is doubt whether a patient is actually using the biological we could better measure the drug-trough level; but –in my practice- this question seldom arises in patients with active arthritis, being treated with a biological.
Measuring drug-trough levels is a completely other item, and perhaps more relevant. Biologicals are in general given in a standard fixed dosage, while there are clear differences in patients characteristics, that could influence bioavailability of the biological. In addition when the disease is more active, it could be that more biological is needed to temper the inflammation compared to low disease activity, where perhaps a lower dosage would be more than effective. To guide physician and patient in personalizing and optimizing treatment with biologicals measuring drug-trough levels might be helpful. Different studies have been performed trying to use through level of the drug in adapting the dosage, and even in predicting possibility to stop the drug treatment. This area is still being evaluated and it is too early to make firm statements, but with a look at cost-effectiveness this will certainly become relevant.
Coming back to the original question: do I use anti-drug antibodies in my daily practice to guide treatment: no, it doesn't influence my decisions. Will I use in the future drug trough levels to guide treatment decisions: this could well be, but it is too early to make a final decision yet.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7118

THURSDAY, 15 JUNE 2017

Which target / outcome is more relevant in the management of SLE?

SP0084 BIOLOGICAL TARGETS IN SLE

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SLE is a prototypical condition characterized by the complete subversion of immunological tolerance and the generation of autoantibodies directed against a wide array of ubiquitous and tissue-specific antigens. This is possible because the joint dysregulation of the innate and adaptive arms of the immune system; which results from multiple gene polymorphisms, each contributing marginally, distinct epigenetic regulation, alteration of the threshold of activation for T and B cells, enhanced responses of antigen-presenting cells resulting from the altered disposal of apoptotic cells, as well as dysregulation of cytokine circuitries including regulatory networks.
Pathogenic mechanisms resulting in clinically overt SLE very likely are heterogeneous among individuals. Thus, the identification of biological targets in SLE goes also with the identification of selected modules of gene activation in distinct individuals. Very strong signals indicate that type I interferon (IFN) may contribute to autoimmunity in a large proportion of SLE individuals and therapeutic trials targeting IFN signaling suggest the clinical relevance of this mediator. B cells/plasmablasts are also relevant and obvious targets. Refinements in our understanding in B cell sub setting and/or the timing in disease development in which they play a relevant role should result in defining the appropriate targets specific to this cell lineage. Gene modules activated during flares suggest that neutrophils in a subset of individuals may also be relevant targets. Cytokine affecting T cell differentiation, in particular T follicular helper cells, represent additional relevant targets.
Within the last several years a number of novel biological targets have been identified in SLE. However, a single biological agent has been approved for SLE treatment in the last five decades. This underlies the difficulties encountered when translating validated targets in efficacious therapeutic agents. This stress the need for careful preclinical evaluation. It further emphasizes the need of small phase II clinical trials based on stringent inclusion criteria aiming at precisely identifying individual groups more likely to respond to validate the target. Current progress made in the identification of molecular signatures in individuals with SLE will offer the tools for the requested accurate selection.
Disclosure of Interest: C. Chizzolini Grant/research support from: Unrestricted reserach grant form GSK
DOI: 10.1136/annrheumdis-2017-eular.7228

SP0085 PATIENT REPORTED OUTCOMES

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In SLE as in other rheumatic diseases, the most relevant target of intervention should be a status with controlled disease process assuring no further accrual of damage. If actual expert discussions like DORIS define the frame of such a status, clinical activity measured by a validated lupus disease activity instrument, serologic activity and therapy – because of harm - are the dimensions of remission with its duration as additional factor for outcome. Patient reported outcomes (PROs) were not included. Otherwise, if payers and reimbursement system decide about relevance, patient outcomes are clear of highest importance as target.
Looking on the evidence of PROs for outcome in SLE, PROs were never used as primary endpoint in clinical trials. In RCTs, PROs were often collected and mostly explorative analysed. There is no evidence that PROs can validly define the above described status of controlled disease. But from systematic analyses in RA, we know that pure PRO like VAS of general health status and semi PRO like tender joints are at least as relevant as more "objective" criteria like swollen joints or CRP as clearly exhibited by the ACR/Eular remission criteria for RA.
The challenge in SLE is that the discrepancies between patients' and physicians' perception and perspectives are even more distinct than in RA. Sometimes, there is the expression that physicians and patients are describing different diseases. The burden of illness in lupus is better defined by pain than by organ manifestations; the overall survival in SLE is more related to lupus nephritis than to fatigue. It is obvious that physicians should analyse the actual clinical symptoms and integrate the future consequences of their actual management in their decision, and patients are more focused on release of their actual burden.
Until today, these different and divers perspectives are no integrated, neither in RCTs nor in daily care. But such integration is mandatory, because no side imagines the complete picture of lupus, which may also produce to the poor results of clinical trials. In routine care, this behaviour causes frustration and mental distress, optimal results are prohibited.
So, the answer to what is more relevant in the management of SLE patients - clinical targets, biological targets or PROs – is the integration of all important aspects of lupus. This implies more than the statistical evaluation of the best items of all three aspects, it is the active involvement of patients in their care: patient empowerment in SLE, a fruitful process, in which both sides have to learn a lot from and about each other.
Disclosure of Interest: M. Schneider Shareholder of: no, Grant/research support from: GSK; UCB, Consultant for: Astra-Zeneca; GSK; Lilly; Roche; Suppremol; UCB, Employee of: no, Paid instructor for: no, Speakers bureau: Astra-Zeneca; GSK; Roche; Pfizer; UCB
DOI: 10.1136/annrheumdis-2017-eular.7248

THURSDAY, 15 JUNE 2017

Joint EULAR - EFIS session: Tilting the balance: from disease to tolerance induction

SP0086 PATHOGENIC MEMORY CELLS: ROAD BLOCKS TO TOLERANCE INDUCTION?

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While conventional state-of-the-art immunosuppression can lead to significant

improvement for patients suffering from rheumatic diseases, only in rare cases a therapy-free remission is achieved. In most cases stopping of treatment results in disease relapse. Apparently, components of the immune system are refractory to conventional immunosuppression and can drive the inflammation. Experimental and clinical evidence suggests that cells of the immunological memory persist despite immunosuppression and if pathogenic play a major role in the chronification of the disease. In particular long-lived memory plasma cells secreting autoantibodies represent a major therapeutic challenge. Once generated, they are not subject to physiological and even conventional therapeutic immune regulation. Their elimination may be prerequisite to curative therapies. A detailed understanding the lifestyle of long-lived memory plasma cells will be important to address this cell type therapeutically.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7257

SP0087 HOW ANTIGEN PRESENTING CELLS CAN BE TURNED INTO TOLEROGENIC CELLS

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Antigen presenting cells (APCs) lay at the heart of all immune responses. Whereas we generally consider APCs as cells that stimulate immune reactivity, they are also critically important for avoiding autoreactivity. Thus in health our tissues are patrolled by cells such as immature dendritic cells, which downregulate responses to self-antigens. Corruption of this process is a central factor in autoimmunity.

A number of groups have developed methods to generate "tolerogenic" antigen presenting cells, that mimic the cells which regulate self-tolerance in health. It is hypothesised that administration of such cells, loaded with autoantigens, to patients with autoimmune disease should be able to overcome autoreactivity and re-establish immune regulation. Our own group has developed a therapeutic approach based upon autologous tolerogenic dendritic cells, which we derive from circulating peripheral blood monocytes. Unlike conventional mature DC, which produce IL-12p70 and other pro-inflammatory cytokines, tolDC produce no IL-12p70 but high levels of IL-10. They deviate naïve T-cells towards an IL-10-producing, anti-inflammatory phenotype and induce hyporesponsiveness in memory T-cells. In mixed cultures they dominate mature, pro-inflammatory DC and down-regulate T-cell activation. Their phenotype is stable in the presence of pro-inflammatory stimuli. Equivalent murine tolDC switch off collagen-induced arthritis, with immune deviation from IL-17 to IL-10 production by CD4+ T cells and a reduction in type II collagen-specific T cell responses.

In a phase 1 trial (AuToDeCRA), we demonstrated that these cells are safe when administered into a recently inflamed target knee joint of patients with inflammatory arthritis. However, in that safety study we were unable to demonstrate a tolerogenic effect in vivo. Furthermore, we have reason to believe that administered cells may remain in the target joint, whereas a disease-modifying effect is likely to require migration to secondary lymphoid tissues. Moving forwards we are designing a study that will address the optimal administration route for tolDC, based on a technique to track the cells in vivo and to measure their effect on autoreactivity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7253

THURSDAY, 15 JUNE 2017

What to do about comorbidity?

SP0088 NEW DRUGS, BUT STILL COMORBIDITY

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As the population ages the simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception. Comorbidity is reported in 35 to 80% of all ill people (Taylor et al. 2010). Comorbidity and multimorbidity are challenging researchers, clinicians and policy makers as these persons require more frequent appointments and hospitalizations and are at a greater risk for drug interactions, disability and mortality (Slater 2011).

Although numerous chronic disease prevention strategies and treatment guidelines have been developed, they mainly address single conditions and ignore the presence of co-existing conditions (van der Noyen 2016). Especially physical activity in its different forms has numerous preventive and curative effects in most of the diseases in addition to drugs. These benefits are such as increased muscle force and aerobic capacity, maintenance of bone and cardiovascular health, decreased inflammation and pain, improved function and well-being.

Studies reveal that more than 80% of rheumatoid arthritis (RA) patients carry two or more comorbid conditions (Krisnan et al. 2005). However, according to the QUEST-RA study (5,235 patients from 21 countries), only 14% of all patients reported to perform physical exercise at least 3 times weekly. Physical inactivity was associated with female sex, older age, obesity, comorbidity, disability, disease activity, pain and fatigue (Sokka et al. 2008). Traditionally, patients with RA were advised to limit physical exercises due to a fear that exercises might increase disease activity and be harmful for joints but more recent studies show that they benefit from exercise (Baillet et al. 2012).

Compared to RA, osteoarthritis (OA) is more common with prevalence of ∼150 million people world-wide. In OA comorbidity rates vary between 68–85% in different studies. The most frequently occurring co-morbidities are diabetes, hypertension, cardiovascular disorders, obesity and back pain. De Rooij et al. (2016) have developed tailored exercise therapy for knee OA and comorbidity. In their study during the 20-week program 76% of the participants needed adaptations to frequency, type, intensity or duration of exercise sessions. In addition, 96% needed education and coaching related to comorbidities.

In our study group-based strength and balance training for two years was offered for community-dwelling participants aged >75 years. The results showed that those who did not start in the group had more comorbidities, lower cognition, higher sedative load, higher risk of malnutrition, and poorer self-reported health than those who started in the gym. Despite of multimorbidity and hospital admissions, many older adults were capable of long-term regular training (Aartolahti et al. 2015).

With multimorbidity multi-drug therapies are common and they increase the risk of side effects. Exercise is also beneficial for health and it should be considered as a non-pharmacological drug. As for any other drugs, individual dosing of exercise is very important as well.

References:

[1] Aartolahti E et al. Gerontol Geriatr.2015;61:452–7.
[2] Baillet A et al. Rheumatology 2012;51:519–527.
[3] de Rooij M et al. Arthritis Care Res. 2016 Aug 26.
[4] Krishnan E et al Ann Rheum Dis. 2005;64:1350–2.
[5] Slater M, BMC Public Health 2011:11:77.
[6] Sokka T et al Arthritis Rheum. 2008:15;59:42–50.
[7] Taylor A et al. BMC Public Health 2010;10:718.
[8] van der Zee-Neuen A Arthritis Care & Research 2016:68,1823–183.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7061

SP0089 HOW TO PREVENT AND TREAT CARDIOVASCULAR COMORBIDITY WITH EXERCISE?

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Low cardiorespiratory fitness is a strong predictor of cardiovascular disease and all-cause mortality in healthy people as well as in patient groups. Unfit individuals have twice the risk of death from all causes, and tailored exercise is important to improve fitness.

It is well established that patients with inflammatory rheumatic diseases have increased risk for cardiovascular disease compared with healthy population, and it is therefore particularly important that these patients benefit from the risk-reducing effect of exercise. Exercise has traditionally been recommended as part of the treatment for patients with rheumatic diseases, but exercise programs has mainly focused on improving mobility and reducing pain. Further, patients with active disease has been recommended to exercise with low intensity. To increase cardiorespiratory fitness, however, high intensity exercise is needed. It is therefore encouraging that recent studies show that patients with active rheumatic disease tolerate intensive cardiorespiratory- and strength exercises and can benefit from such health-enhancing training. Recent research in this field will be presented and discussed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7287

SP0090 COMORBIDITY-ADAPTED EXERCISE FOR PATIENTS WITH KNEE OSTEOARTHRITIS

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Exercise therapy is a key intervention in the management of patients with knee OA[1]. However, comorbidity is present in 68 to 85% of patients with OA (e.g. cardiac disease, diabetes type 2, obesity)[2,3]. Comorbidity interferes with exercise therapy. In clinical practice, comorbidity is a frequent reason to exclude patients from exercise therapy. If accepted into an exercise program, both therapists and patients tend to reduce exercise intensity to a level unlikely to be effective, because of fear of aggravating symptoms of the comorbid disease. Further, the effect of exercise therapy in patients with knee OA and severe comorbidity is not known. Patients with unstable medical conditions, precluding safe participation in an exercise program, are excluded from clinical trials. In view of the effectiveness of exercise therapy in knee OA and the high prevalence of comorbidity, there is a great need for comorbidity-related adaptations to exercise therapy. In this lecture a strategy (i3-S strategy) will be presented on how to develop comorbidity-related adaptations to exercise therapy in an index disease (e.g osteoarthritis)[4]. According this strategy we have developed a tailored exercise program for patients with knee OA and comorbidity. Subsequently, to evaluate the efficacy of the tailored exercise program for patients with knee OA and comorbidity (cardiac disease, diabetes type 2, COPD and obesity (body mass index $\geq$30kg/m^2) a randomized controlled trial (n=126) was performed in a secondary care setting. The results showed that tailored exercise therapy greatly improved physical functioning, reduced pain and