are designed to kill cells, ICI block interactions that regulate the T cell response to cancer. At present, two classes of ICI are available to treat a wide variety of malignancies: antibodies to cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and antibodies directed to the programmed death-1 (PD-1) and PD-1 ligand (PD-L1) axis, either to PD-1 or PD-L1. While both anti-CTLA-4 and antibodies to PD-1/PD-L1 are effective, these systems differ in the T cell populations affected, the location of these cells and the downstream signaling pathways involved. ICI can be used alone or in combination. Despite differences in mechanism of action, treatment with both types of ICI is associated with severe side effects that have been termed immune-related adverse reactions (irAE). irAE include, among other manifestations, dermatitis, colitis, pneumonitis, endocrinopathy (hypothyroidism, hypophysitis, adrenal insufficiency) and arthritis and related conditions. Because of the goal of ICI therapy is the induction or stimulation of cytotoxic T cells, the effect of these agents on B cells has received much less attention. In general, effects of ICI on tumors are considered the action of T cells. irAE, however, may result from B cell effects and the induction of autoantibodies. Thus, autoantibodies to thyroid antigens may lead to thyroiditis and subsequent hypothyroidism. Similarly, ICI can lead to the production of antibodies to islet antigens as well as glutamic acid decarboxylase 65 and induction of diabetes. On the other hand, while arthritis can be an irAE, affected patients usually do not show antibodies to citrullinated proteins (ACPA). Importantly, functional and phenotypic properties of B cells following ICI may help predict the emergence of irAE. Much of the data on this issue comes from a detailed analysis of patients with melanoma treated with anti-CTLA-4, anti-PD-1 or the combination. With this combination, B cells of treated patients showed characteristic changes that include a decrease in the number of circulating B cells in conjunction with an increase in plasmablasts and a population of B cells characterized by low expression of CD21. Furthermore, in treated patients, the CD21^{lo} B cells population showed greater clonality as well as a higher frequency of clones in comparison to the CD21^{hi} population. These changes, which may resemble those seen in patients haploinsufficient for CTLA-4, may predict the development of irAE. The CD21^{lo} B cell population may have a particular role in the development of irAE since these cells appear to be recent emigrants from germinal centers and may undergo rapid activation. The effects of ICI on B cell populations is also relevant for ICI use in the setting of pre-existent inflammatory or autoimmune disease marked by autoantibody production. While ICI, either alone or in combination, can lead to the exacerbation of these conditions, the effect on autoantibody production has not yet been well studied. These exacerbations, however, can respond to agents such as glucocorticoids or TNF blockers whose B cell effects are not clear. Since B cells can express PD-1 as well as PD-L1, the effects of ICI may direct actions or the indirect effects on other cell populations. Future studies are needed to delineate more precisely the contribution of B cells to the response of cancer to ICI as well as the development of irAE.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Orthotic treatment: is it in or out?

SP0178 LOWER LIMB ORTHOSES

Martin van der Esch. Amsterdam Rehabilitation Research Center | Reade, Rehabilitation, Amsterdam, Netherlands

Background: Osteoarthritis (OA) is the most common rheumatic disease of the musculoskeletal system, with the knee as the most affected joint. The number of people with OA of the knee is likely to increase due to the ageing society and the obesity epidemic. The predominant clinical symptom of knee OA is pain, which is described as worsening by activity and relieving by rest. Knee instability has been recognized as an important clinical feature in persons with knee OA. Pain and knee instability are associated with limitations in performing daily activities. Non-pharmacological options in the management of knee OA consist of education, weight loss, exercise, braces and physical therapy. Knee bracing has been recommended by the Osteoarthritis Research Society International (OARSI). Valgus knee braces designed to decrease loads on the medial compartment of the knee for patients with varus alignment are the most common. It has been shown however, that valgus bracing may have little or no effect on pain and physical functioning, and adherence to this treatment in patients with knee OA is low.

Because of ease of use and access, lack of complications and low cost, soft knee braces are commonly used in persons with knee OA. However, the evidence for efficacy of soft knee bracing on pain and activity limitations in knee OA is limited. Therefore, it is important to strengthen the evidence of using a soft brace to reduce pain and activity limitations as well as to evaluate the efficacy of soft knee bracing on knee instability in persons with knee OA. There is also debate about the

effectiveness of soft braces in other affected joints of the lower extremity and in conditions other than OA such as rheumatoid arthritis.

Objectives: The aim of the study will be to evaluate the effect of wearing a soft brace on dynamic knee instability in patients with OA of the knee.

Methods: Persons with knee OA and self-reported knee instability from the Amsterdam Osteoarthritis cohort participated in a single-session lab-experimental study. A within-subject design was used, comparing no brace versus brace, and comparing a non-tight versus a tight brace (standard fit). The primary outcome measure was dynamic knee instability, expressed by the Perturbation Response (PR), i.e., a biomechanics based measure reflecting deviation in the mean knee varus-valgus angle after a controlled mechanical perturbation, standardized to the mean (SD) varus-valgus angle during level walking. Linear mixed-effect model analysis was used to evaluate the effect of a brace on dynamic knee instability.

Results: The wearing of a soft brace reduced the knee instability significantly during perturbed walking. Results will also be presented from the literature search and from the lab-experimental study.

Conclusion: Wearing a soft brace reduces dynamic knee instability in patients with knee OA. However, longitudinal studies are needed to evaluate the clinical implications of wearing a soft brace.

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SP0179 ORTHOSES AND ASSISTIVE DEVICES FOR THE HAND

Nina Osteras. Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway

This presentation will summarize the scientific evidence for the effects of orthoses and assistive devices for the hand. The main focus will be on hand osteoarthritis. The presentation will shed light on how orthoses and assistive devices may facilitate participation.

Disclosure of Interests: None declared

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SP0180 FOOT ORTHOSES IN RA

Jim Woodburn. Glasgow Caledonian University, School of Health and Life Sciences, Glasgow, United Kingdom

In this presentation I will: (1) Provide a general overview of the indications and use of foot orthoses in rheumatoid arthritis (RA) ¹, (2) Explore mechanisms of action with respect to preserving, maintaining and restoring foot biomechanics ², (3) Summarise current evidence on the use of foot orthoses for managing foot pain, disability, deformity and quality of life by drawing on recently published systematic reviews and meta-analyses³. Further I will direct delegates to national, European and International evidence-based clinical guidelines where they exist^{1,4}, and (4) Introduce new technology advances with regards to materials and digital design and manufacturing concepts².

I will conclude the presentation by setting out future directions and priorities for both clinical practice and research and innovation.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Current treatment of vasculitis

SP0181 TREATMENT OF GCA

John H. Stone. USA

The treatment of giant cell arteritis (GCA) has taken a dramatic leap forward over the past 18 months, with the start of the era of interleukin-6 inhibition for the treatment of this disease. For the first time in 70 years, rheumatologists now have a highly-effective alternative to continuous therapy with doses of glucocorticoids that are often unacceptably high, leading inevitably to steroid-related toxicity. Clinicians now have many questions about the optimal approach to treatment in this new era: When should IL-6 inhibition begin? How quickly should glucocorticoids be tapered? Should prednisone be stopped completely? Can tocilizumab ever be discontinued? How does one monitor for the possibility of disease flare? This session will address all of these questions using a data-driven approach, with reference to new data from the GACTA trial

Disclosure of Interests: John H. Stone Grant/research support from: F. Hoffmann-La Roche, Genentech, Xencor, Consultant for: Chugain, F. Hoffmann-La Roche, Genentech, Xencor

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SP0182 TREATMENT OF AAV

David Jayne. University of Cambridge, Department of Medicine, Cambridge, United Kingdom

Background: ANCA associated vasculitis is an autoimmune disease classified by clinical phenotype and serology. A genetic predisposition has been determined which differs between PR3-ANCA and MPO-ANCA patients. Experimental models have confirmed the pathogenicity of ANCA for certain aspects of pathology and have defined a role for alternative complement pathway activation but have failed to explain granuloma formation or gain insights into the origin of breakdown of tolerance. Therapy has emerged empirically to include the combination of high dose glucocorticoids and immunosuppression with B cell depletion, Rituximab, emerging as an alternative immunomodulator over the last 20 years. Studies have evaluated the role of Rituximab in induction, in refractory and relapsing disease and in the prevention of relapse and have explored the role of biomarkers in monitoring therapy. AAV patients continue to suffer poor outcomes especially if renal, cardiac or gastrointestinal features are present at diagnosis. Adverse event rates remain high and the majority of patients pursue a relapsing course. Inhibition of the alternative complement component C5a is emerging as a new therapeutic opportunity.

Objectives: To define the outcomes and predictors for adverse outcomes in AAV. To review recent clinical trial data in the context of established guideline statements and to discuss the treatment of more complex clinical scenarios.

Methods: A description of current approaches to classification and subgrouping by severity. Review of recent clinical trial data and guidelines and application of learned knowledge to clinical scenarios.

Conclusion: AAV remains a disease with poor outcomes. There is a need for further understanding of the barriers to early diagnosis and access to specialist care. Treatment decisions are now well supported by evidence from clinical trials. Rituximab has had a major influence on current management strategies and is leading to improved outcomes and reduced glucocorticoid exposure. Complement inhibition is a potential new therapy for AAV.

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SP0183 DIAGNOSIS AND TREATMENT OF HCV RELATED VASCULITIS

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Chronic hepatitis C virus (HCV) infection is the most common cause of cryoglobulinemic vasculitis. In contrast, non-cryoglobulinemic vasculitis is rare in chronic HCV infection. Cryoglobulinemic vasculitis is a systemic immune complex-mediated vasculitis predominantly affecting small vessels and associated with the presence of serum cryoglobulins, i.e. cold-precipitable immunoglobulins. HCV is a hepato- and lymphotropic virus. Notably, secondary transition from benign lymphoproliferative disease to malignant non-Hodgkin lymphoma (NHL) as well as primary co-manifestation of cryoglobulinemic vasculitis and NHL has been reported in chronic hepatitis C. While cryoglobulinemia is detected in 50% or more of the patients with chronic hepatitis C, less than 5% develop related vasculitis. In this disorder, HCV induces clonal proliferation of memory phenotype marginal zone-like B-lymphocytes with restricted Ig heavy chain variable (V_H) 1-69 gene expression encoding for the IgM rheumatoid factor (RF) WA idiotype. Monoclonal IgM RF binding to the Fc region of polyclonal IgG with anti-HCV reactivity facilitate the formation of cryoprecipitable multi-molecular immune-complexes. Cryoglobulins are preferentially deposited in tissues with high blood flow per unit mass of tissues, e.g. skin, synovium, choroid plexus and glomerulus, where they bind to endothelial cells via the C1q receptor.

Endothelial cryoglobulin deposition induces the activation and recruitment of circulating neutrophil granulocytes and other immune cells to the endothelial lesion eventually resulting in complement-consuming vasculitis.

The histopathologic changes in HCV-related vasculitis range from cutaneous leukocytoclastic vasculitis to severe necrotizing arteritis. Type I membranoproliferative glomerulonephritis is frequently found in patients with renal involvement. Clinical features of HCV-associated vasculitis comprise purpura, Meltzer's triad (purpura, arthralgia, asthenia), polyneuropathy, renal involvement and Raynaud's