# Lower limb orthoses

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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 haploinsufficent 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: T**he 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.

**REFERENCE:**

[1] Cudejko T, van der Esch M, Schrijvers J, Richards R, van den Noort JC, Wrigley T, van der Leeden M, Roorda LD, Lems W, Harlaar J, Dekker J. The immediate effect of a soft knee brace on dynamic knee instability in persons with knee osteoarthritis. Rheumatology (Oxford). 2018 Oct 1;57 (10):1735-1742.

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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.

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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-analyses[3]. 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 concepts[2].
I will conclude the presentation by setting out future directions and priorities for both clinical practice and research and innovation.

**REFERENCES:**

[1] Hennessy K, Woodburn J, Steultjens M. Clinical practice guidelines for the foot and ankle in rheumatoid arthritis: a critical appraisal. J Foot Ankle Res. 2016 Aug 19;9:31.
[2] Gibson KS, Woodburn J, Porter D, Telfer S. Functionally optimized orthoses for early rheumatoid arthritis foot disease: a study of mechanisms and patient experience. Arthritis Care Res (Hoboken). 2014 Oct;66(10):1456-64.
[3] Hennessy K, Woodburn J, Steultjens MP. Custom foot orthoses for rheumatoid arthritis: A systematic review. Arthritis Care Res (Hoboken). 2012 Mar;64(3):311-20.
[4] Chapman LS, Redmond AC, Landorf KB, Rome K, Keenan AM, Waxman R, Alcacer-Pitarch B, Siddle HJ, Backhouse MR. Foot orthoses for people with rheumatoid arthritis: a survey of prescription habits among podiatrists. J Foot Ankle Res. 2019 Jan 25;12:7.