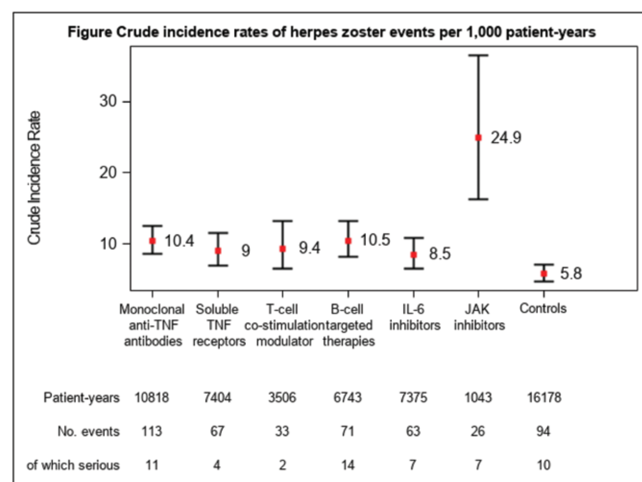
Table. Risk of herpes zoster: Results of adjusted regression analyses with and without inverse probability weights

	Multivariate Analysis without IPW		Multivariate Analysis with IPW	
	Adjusted HR (95% CI)	P Value	Adjusted HR (95% CI)	P Value
Female sex	1.42 (1.12-1.82)	**0.0042**	1.21 (0.96-1.53)	0.1095
Age per 10 years	1.23 (1.13-1.33)	**<.0001**	1.31 (1.2-1.43)	**<.0001**
Glucocorticoids, 5-10 vs 0 mg/d	1.16 (0.95-1.41)	0.1577	1.23 (1-1.52)	0.0501
Glucocorticoids, >10 vs 0 mg/d	1.58 (1.02-2.46)	**0.0417**	1.92 (1.27-2.92)	**0.0022**
csDMARD treatment	*Reference*		*Reference*	
Monoclonal TNFi antibodies	1.55 (1.20-2.00)	**0.0009**	1.63 (1.25-2.12)	**0.0003**
Soluble TNF receptors	1.32 (0.98-1.77)	0.0683	1.34 (0.98-1.83)	0.0631
T-cell co-stimulation modulator	1.41 (0.97-2.05)	0.0746	1.69 (1.17-2.45)	**0.0048**
B-cell targeted therapies	1.45 (1.07-1.97)	**0.0156**	1.66 (1.19-2.3)	**0.0026**
IL-6 inhibitors	1.31 (0.97-1.77)	0.0737	1.55 (1.15-2.09)	**0.0045**
JAK inhibitors	3.55 (2.33-5.41)	**<.0001**	5.01 (3.45-7.28)	**<.0001**



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Preclinical models of arthritis and bone disease

OP0239 WHY DOES ALCOHOL INHIBIT ARTHRITIS? - AN EXPLANATION OF THE MECHANISM OF ARTHRITIS INHIBITION BY ETHANOL

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Background: Alcohol consumption has emerged as consistent protective factor for the development of autoimmune diseases such as rheumatoid arthritis (RA). The underlying mechanism for this tolerance-inducing effect of alcohol, however, is unknown.

Objectives: To understand the anti-arthritogenic effect of alcohol

Methods: The immune-regulatory properties of alcohol consumption in vivo were tested in the collagen-induced arthritis (CIA) and serum-induced arthritis (SIA) model as well as after immunization with T cell- dependent (NP-CGG) and independent (TNP-FICOLL) antigens. Additional experiments in vivo experiments in these models were done with acetate- the metabolite of ethanol. The models were analysed for T- cell lineage and plasma cell differentiation, germinal centre formation and IgG levels and sialylation. Molecular expression of T follicular helper cell (TFH) activation such as IL-21, Bcl-6 and PD-1, as well as TFH: B cell conjugates were also assessed. Furthermore, TFH cells were generated in vitro, exposed to ethanol or acetate and tested for IL-21 production, PD1 expression and conjugate formation with B cells.

Results: Ethanol exposure significantly inhibited arthritis in the active adaptive immunity-driven model of arthritis (CIA) but not in the passive innate immunity-driven model (STA) suggesting that the immune suppressive effect of alcohol is based on interference of T- and B- cell activation. In line ethanol and even more its metabolite acetate, suppressed T cell dependent antibody formation after NP-CGG immunization, while T cell independent antibody formation after TNP-FICOLL immunization was not suppressed. Ethanol, as well as its metabolite acetate, specifically altered the functional state of T follicular helper (T_{FH}) cells in vitro and in vivo, thereby exerting immune regulatory and tolerance-inducing properties. Alcohol-exposed mice showed reduced Bcl6 and PD-1 expression as well as interleukin (IL)-21 production by TFH cells, preventing proper spatial organization of TFH cells to form TFH: B cell conjugates in the germinal centre. This effect of alcohol on T_{FH} cells was associated with impaired autoantibody formation, higher sialylation of autoantibodies and less arthritis. In accordance, overexpression of IL-21 in vivo completely reversed the immune regulatory effects of alcohol.

Conclusion: In summary, these data provide a new mechanistic explanation for the immune regulatory and tolerance-inducing effect of alcohol consumption in arthritis.

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OP0240 A MULTIMODAL MASS SPECTROMETRY APPROACH REVEALS SPECIFIC CARTILAGE MOLECULAR PROFILES ASSOCIATED TO TYPE 2 DIABETIC PATIENTS

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Background: Osteoarthritis (OA) is mainly characterized by the progressive deterioration of articular cartilage. Recent studies support that type 2 diabetes (TD2) is a risk factor to develop OA [1, 2]. However, the molecular cartilage profile of patients combining these two diseases remains unclear, and a better understanding of the different OA phenotypes should be considered for the development of personalized medicine.

Matrix-assisted laser desorption/ionization (MALDI) mass spectrometry imaging (MSI) is used to investigate the bimolecular distribution of proteins, lipids or metabolites through the *in-situ* analysis of tissue sections. Bottom-up proteomics focuses on the relative quantification of proteins. The combination of both technologies could be considered to reveal specific molecular profiles and help for patient classification.

Objectives: The main goal of this study is to apply a multimodal mass spectrometry approach on cartilage to reveal specific lipidomic and proteomic profiles associated to TD2 patients.

Methods: Human cartilages from OA (n_a=10) and OA/TD2 human patients (n_b=10) were obtained from donors undergoing total knee joint replacement. Cartilage punches of 8*8mm were sectioned at 12 µm thickness for MALDI-MSI and bottom-up proteomics.

For MALDI-MSI experiments (n_a=6; n_b=6), norharmane matrix was sprayed over the samples for the detection of lipids. Experiments were then performed in positive ion polarity at 50 µm of lateral resolution using a RapifleX MALDI

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