

## Poster Session 1 - Oral Presentations

## O01-P045

## Whole-genome imputation study implicates TLR2 locus variants that confer risk for Behçet's disease by increasing innate immune response against microbes

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**Introduction.** Several Behçet's disease susceptibility genes have been identified by genome-wide association studies (GWASs). Early GWASs identified genes involved in adaptive immunity such as *HLA class I*, *IL10*, *IL23R*, *IL12RB2*, *STAT4* and *ERAP1*. More recent genetic findings have emphasized importance of genes participating in innate immunity and pathways of host defense, including *MEFV*, *IL1A-IL1B*, *IRF8*, *RIPK2*, and *FUT2*.

**Aims.** To discover new genetic loci that contribute to Behçet's disease, we conducted whole-genome imputation of the Turkish genome-wide association study.

**Methods.** Genomic data from a genome-wide association study, including 311,459 markers in 1,278 patients with Behçet's disease and 1,215 healthy controls from Turkey, were used to impute genotypes of over 5.9 million markers. Loci with  $P < 5 \times 10^{-6}$  were directly genotyped in a replication cohort of 769 patients and 601 healthy controls from Turkey. TNF was measured in supernatants of healthy control peripheral blood mononuclear cells after stimulation with the *TLR2* ligand, zymosan. The cells were genotyped for the *TLR2* disease risk SNP.

**Results.** In total, 5,927,016 markers were analyzed. There were 13 novel loci, which showed at least suggestive associations ( $P < 5 \times 10^{-6}$ ), Figure 1. Lead SNPs from each novel locus were selected and genotyped in the Turkish replication cohort. A SNP rs11724697 located in *CPLX1* was identified with genome-wide significance ( $p = 3.33 \times 10^{-8}$ ), however, did not reach significance in the replication cohort. A risk allele of rs1869947 in *TLR2-RNF175* showed strong association in both cohorts and meta-analysis revealed genome-wide association ( $p = 8.01 \times 10^{-9}$ , OR 1.64, 95% CI 1.38-1.94). Zymosan-stimulated peripheral blood mononuclear cells homozygous for the risk allele of rs1869947 produced more tumor necrosis factor (TNF) protein than cells from protective allele homozygotes ( $p = 0.025$ ).

**Conclusion.** This study identified *TLR2-RNF175* as a susceptibility locus for Behçet's disease with genome-wide significance. Our findings suggest that increased production of TNF through Toll-like receptor 2 pathway signaling in response to microbial products has a key role in pathogenesis of disease.

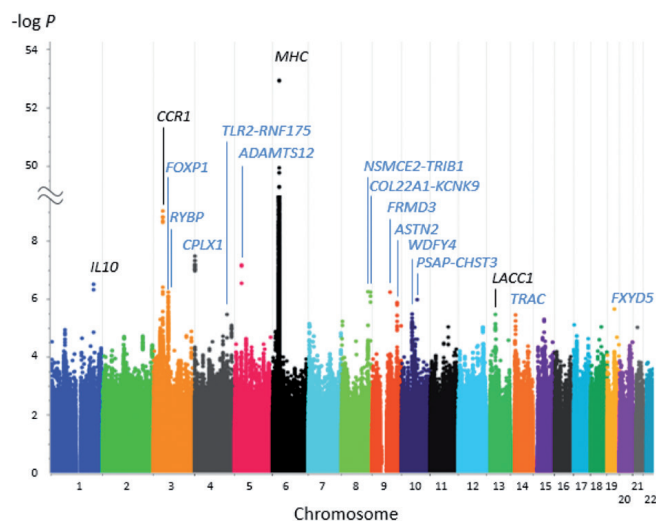


Fig. 1. Association of imputed markers.

## O02-P039

## A comparative study about ERAP1 polymorphisms in Behçet syndrome and ankylosing spondylitis Italian patients

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**Introduction.** The Endoplasmic reticulum aminopeptidase protein 1 (ERAP1) trims N-terminal amino acids from epitope precursors for Major Histocompatibility Complex (MHC) class I presentation. Genome-wide association studies (GWASs) demonstrated that *ERAP1* single nucleotide polymorphisms (SNPs) are associated with several diseases, including Behçet syndrome (BS) and Ankylosing Spondylitis (AS). *ERAP1* SNPs effect on disease susceptibility has been related to the different disease-associated MHC-I interacting with ERAP1 (1-4).

**Aims.** The aim of our study was to genotype the most significant non-synonymous *ERAP1* tagSNPs: rs30187 (NG\_027839.1:g.30519A>G; NP\_057526.3:p.Lys528Arg), rs17482078 (NG\_027839.1:g.35983G>A; NP\_001035548.1:p.Arg725Gln) and rs27044 (NG\_027839.1:g.35997C>G; NP\_001035548.1:p.Gln730Glu). We also aim to compare the variants distribution in BS and AS Italian patients.

**Methods.** We recruited a total of 104 Italian subjects, including 51 BS (29 male:22 female; mean age: 46 years, range: 25-76 years), and 53 AS patients (35 male:18 female; mean age: 47 years, range: 18-78 years), at Rheumatology Institute of Lucania (IREL). Genomic DNA was isolated from subject's whole blood by standard procedures and screened for *ERAP1* tagSNPs. *In vitro* amplification (PCR) and direct sequencing were used for the molecular investigations. Upstream *in silico* analysis was performed for target-specific primers design using NCBI Primer-Blast tool. Downstream computational analysis was also carried out, querying BlastN on line tool for similarity analysis (compared to NG\_027839.1 NCBI Reference Sequence) and Mutation surveyor software for gene variant analysis. The differences in genotype frequencies BS and AS patients were analysed using the chi-square test ( $p$ -values  $< 0.05$  were considered significant).

**Results.** SNPs genotyping results were shown in Table I. A statistically significant difference was observed for both heterozygous and mutant homozygous genotypes of rs30187 when BS and AS patients were compared. In detail, the heterozygous condition was more frequent in AS group, while the homozygosity was higher in BS group. The rs17482078 AA mutant genotype was absent in AS group, while its frequency was about 19% in BS cohort. The frequency of rs17482078 SNP in heterozygosity state showed no statically significant difference between the groups. No differences were also found for the rs27044 variant when BS and AS patients were compared.

Table I. ERAP1 SNPs distribution in BS and AS patients.

SNP ID	Amino acid change	Genotype	BS patients (n=51) n (%)	AS patients (n=53) n (%)	p-value
rs30187	Lys528Arg	AA	19 (37.25)	12 (22.64)	NS
		AG	12 (23.53)	38 (71.70)	<0.01
		GG	20 (39.22)	3 (5.66)	<0.01
rs17482078	Arg725Gln	GG	26 (50.98)	40 (75.47)	NS
		GA	15 (29.41)	13 (24.53)	NS
		AA	10 (19.61)	0 (0.00)	<0.01
rs27044	Gln730Glu	CC	11 (21.57)	12 (22.64)	NS
		CG	14 (27.45)	23 (43.40)	NS
		GG	26 (50.98)	18 (33.96)	NS

Abbreviations: SNP, single nucleotide polymorphism; BS, Behçet syndrome; n, number of subjects; AS, ankylosing spondylitis

**Conclusion.** A different distribution of the most significant *ERAP1* coding variants within BS and AS patients groups was found. Although a significant difference was observed in rs30187 genotype distribution, we can notified that the variation is frequent in both groups of patients, accordingly to its role in influencing the protein structure and activity. The rs17482078 frequency is higher within BS group compared with AS group. According to the literature, this SNPs is associated with BS risk, but the same is protective against AS. These data need to be tested in larger genetic studies in order to confirm our findings.

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## O03-P017

**Chemokine receptor CCR1 and its ligand CCL3 in a mouse model of Behçet's disease**

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**Introduction.** Although gene variants of CC chemokine receptor type 1 (CCR1) have been reported, the protein expression of CCR1 in Behçet's disease (BD) patients remains unclear.

**Aims.** The objective of this study is to analyze the frequencies of CCR1+ cells in herpes simplex virus-induced mouse model of BD.

**Methods.** The frequencies of CCR1+ cells on the surface and in the cytoplasm of peripheral blood leukocytes and lymph nodes were analyzed by flow cytometry.

**Results.** The CCR1+ cells were significantly down-regulated in BD mice compared with the normal control and symptom-free control mice. Colchicine and pentoxifylline treatment improved the symptoms of BD and increased the frequencies of CCR1+ cells in BD mice. Treatment with chemokine CC motif ligand 3 (CCL3), a ligand of CCR1, deteriorated BD symptoms in 10 of 16 BD mice (62.5%) via down-regulation of CCR1+ cells. Anti-CCL3 antibody treatment ameliorated BD symptoms in 10 of 20 mice (50%) and significantly decreased the disease severity score compared with CCL3-treated BD mice ( $p=0.01$ ) via up-regulation of CCR1+ cell frequencies.

**Conclusion.** These results show that the up-regulation of CCR1+ cells was related to the control of systemic inflammation of BD in a mouse model.

## O04-P041

**The combination of a low expressing KIR3DL1 allotype and KIR3DS1 contributes toward the risk of developing Behçet's disease**

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**Introduction.** Behçet's disease is a chronic, relapsing-remitting autoinflammatory syndrome with a strong HLA-B\*51 association (1). HLA-B\*51 is known to interact with KIR3DL1 via the Bw4 epitope (2). Over one hundred alleles of KIR3DL1 have now been described, however to date, there is no data regarding the relationship between specific KIR3DL1 allotypes or combinations of allotypes and Behçet's disease.

**Aims.** We aimed to investigate HLA-A, -B and KIR3DL1 associations in a large cohort of patients with Behçet's disease

**Methods.** We describe a cohort of 267 individuals with Behçet's Disease and 445 matched healthy controls from a tertiary referral centre in the United Kingdom. Patients underwent clinical phenotyping by a panel of six Behçet's Disease experts. Genomic DNA was extracted from peripheral blood and sequenced using a panel of amplicons designed to amplify HLA-B and KIR3DL1. HLA-A was analysed using sequence specific oligonucleotide probes (Immucor, Peachtree Corners, GA, USA). HLA-B alleles were assigned using the NGS-Engine software package (GenDx, Utrecht, Netherlands). KIR3DL1 alleles were assigned using the PING pipeline (3). odds ratios and p values were adjusted for multiple testing.

**Results.** HLA-B\*51 was confirmed as a genetic risk factor in this group ( $p=0.0006$ ,  $pc=0.0192$ , OR 1.92, 95% CI 1.33-2.76). KIR3DL1/S1 allele-level analysis indicated that low-expressing KIR3DL1/S1 alleles in combination with KIR3DS1 increased the risk of developing Behçet's disease (KIR3DL1LOW/KIR3DS1:  $p=0.0004$ ,  $pc=0.0040$ , OR 2.47, 95% CI 1.43-4.25), whereas high-expressing KIR3DL1/S1 alleles in combination with a null-expressing KIR3DL1 reduced the risk of disease (KIR3DL1HIGH/KIR3DL1NULL:  $p=0.0035$ ,  $pc=0.0350$ , OR 0.53, 95% CI 0.33-0.87). Behçet's disease can manifest as a purely mucocutaneous disease or can involve other organ systems such as the eyes. In the UK cohort studied here, KIR3DL1LOW/KIR3DS1 increased the risk of ophthalmic disease ( $p=1.2 \times 10^{-5}$ , OR 3.92, 95% CI 2.06-7.47), whereas KIR3DL1HIGH/KIR3DL1NULL provided protection against mucocutaneous disease ( $p=0.0048$ , OR 0.45, 95% CI 0.25-0.81).

**Conclusion.** This is the first analysis of KIR3DL1/S1 allelic variation in Behçet's Disease and may provide insight into the pathogenic role of HLA-B\*51 and its interaction with KIR3DL1/S1. Our work follows on from previous attempts to investigate the functional effects of HLA-B\*51 in Behçet's Disease. These findings suggest that KIR3DL1 may be involved in the pathogenesis of the disease via mechanisms other than Bw4 interactions – such as the newly characterised interaction of KIR3DS1 with HLA-F (4).

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## O05-P028

**Clustering analysis of Japanese Behçet's disease identifies intestinal type as distinct cluster**

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**Introduction.** Patients with Behçet's disease (BD) present with various clinical symptoms, with different disease outcomes. Recently, rapid increment of intestinal BD has been reported in Japan (1), whereas intestinal BD is rare in Middle East. Subgrouping analysis with BD patients had been performed mostly in Turkey (2). However, BD patient characteristics depend largely on geographic area, and thus clustering analysis in Japan is also warranted.

**Aims.** We performed a subgrouping analysis in an attempt to identify a predictive factor for the treatment and prognosis of BD in Japan.

**Methods.** We performed a principal component analysis (PCA) of 691 BD patients, mostly fulfilling the Japanese Ministry of Health, Labor and Welfare criteria (294 males and 397 females) in 7 hospitals from the year 1991 to 2017. We analyzed patient's clinical symptoms (oral ulceration, genital ulceration, eye lesion, skin lesion, neurological lesion, intestinal lesion, vascular lesion) as a variable. PCA was performed with SPSS version 22.0 (IBM Japan).

**Results.** PCA extracted three significant components; Group A: patients having eye or neurological lesions without vascular and intestinal lesions (362 cases), Group B: patients having vascular or intestinal lesions without eye and neurological lesions (91 cases) and Group C: patients without eye and special type of BD (190 cases). When we compared the three groups, there were significantly more men in Groups A (51.9%) and B (45.0%), more HLA-B51 positive cases in Groups A (37.8%), more cases with biologics in Group A (16.9%) and B (18.7%), and more complete type of BD in Group A (46.9%) by chi-square test ( $p<0.05$ ). We found a significant trend in reduction of Group A (57.8% before 2000, 50.0% in 2000–2007, and 44.0% in 2008–2017), and increment of Group B (9.4% before 2000, 15.2% in 2000–2007, and 18.7% in 2008–2017).

**Conclusion.** We identified three distinct subgroups in BD with PCA, and there is a significant difference in patient's background, clinical characteristics, and treatment between subgroups. Group B BD is rapidly increasing in Japan.

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## O06-P049

**Disease activity and quality-of-life improvements in patients with Behçet's syndrome: a phase III randomized, placebo-controlled, double-blind study of apremilast (RELIEF)**

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**Introduction.** Oral ulcers, the hallmark of Behçet's syndrome, can be painful and disabling, impairing the quality of life (QoL) in patients with Behçet's syndrome. Apremilast, an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in a phase II placebo-controlled study in patients with Behçet's syndrome and active oral ulcers. Moreover, a phase III study showed improvement in number and pain of oral ulcers as well as disease activity in patients with Behçet's syndrome and active oral ulcers previously treated with  $\geq 1$  medication.

**Aims.** To assess the effects of apremilast on patient-reported outcomes, including measures of disease activity and QoL, in patients with Behçet's syndrome enrolled in a phase III randomized, placebo-controlled, double-blind study.

**Methods.** Eligible patients (N=207) were randomized (1:1) to apremilast 30 mg twice daily (n=104) or placebo (n=103) for 12 weeks, followed by a 52-week active-treatment extension. Patients had active Behçet's syndrome, with  $\geq 3$  oral ulcers at randomization or  $\geq 2$  oral ulcers at screening + randomization, without active major organ involvement. The primary endpoint was area under the curve (AUC) for total number of oral ulcers over 12 weeks.

The clinical improvement of oral ulcers was evaluated by assessments of oral ulcer pain, measures of disease activity, and QoL. Disease activity was measured using validated instruments that take into account other manifestations of Behçet's syndrome involving the skin, joints, gastrointestinal tract, eyes, central nervous system, and vascular involvement. These included the Behçet's Disease Current Activity Index Form (BDCAF), which consists of 3 components, and the Behçet's Syndrome Activity Score (BSAS). QoL was assessed using the Behçet's Disease QoL (BDQoL) questionnaire. BSAS and BDQoL were completed by the patients and the BDCAF was administered to the patients by the investigator. A prespecified hierarchical testing procedure was used for multiplicity adjustment.

**Results.** The primary endpoint of the AUC for number of oral ulcers over 12 weeks was statistically significantly lower in the apremilast group compared with the placebo group. This treatment effect is supported by the statistically significant improvements observed in oral ulcer pain, measures of disease activity using the BSAS and BDCAF (Behçet's Disease Current Activity Index [BDCAI] and Patient's Perception and Clinician's Perception, respectively) and the BDQoL at Week 12 (Table).

Table

Endpoint	P Value	Adjusted Treatment Difference	Apremilast vs. Placebo (LS Mean)
AUC for the number of oral ulcers from baseline through Week 12	<0.0001	-92.6	129.5 vs. 222.1
Change from baseline in the pain of oral ulcers as measured by 100 mm VAS at Week 12	<0.0001	-24.8	-40.7 vs. -15.9
Change from baseline in BSAS at Week 12	<0.0001	-11.94	-17.35 vs. -5.41
Change from baseline in BDCAF components at Week 12			
BDCAI	0.0335	-0.5	-0.9 vs. -0.4
Patient's Perception of Disease Activity	<0.0001	-1.0	-1.7 vs. -0.7
Clinician's Overall Perception of Disease Activity	<0.0001	-0.9	-1.6 vs. -0.7
Change from baseline in BDQoL at Week 12	0.0003	-3.0	-3.5 vs. -0.5

The incidence of treatment-emergent adverse events (AEs) was comparable between the apremilast and placebo groups during the placebo-controlled period (78.8% vs. 71.8%, respectively). Serious AEs were observed in 3

apremilast patients (migraine, oral ulcer flare, genital ulcer, arthralgia, soft tissue injury) and 4 placebo patients (diarrhea, genital and fungal infections, oral ulcer flare, acne, acute febrile neutrophilic dermatosis, erythema multiforme).

**Conclusion.** This phase III study demonstrated the efficacy of apremilast in the reduction of oral ulcers. Patients reported improvements in oral ulcer pain, disease activity measures, and QoL. These findings suggest that reduction in oral ulcer is associated with improvement in overall disease activity and QoL reported by patients. The safety profile was consistent with the known safety profile of apremilast.

## O07-P034

**Pediatric Behçet's disease; report of 204 cases from the Iran registry of Behçet's disease**

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**Introduction.** Pediatric Behçet's disease (PED-BD) is a well-recognized form of the disease with different presentation in various parts of the world.

**Aims.** To report the characteristics of PED-BD in a cohort of patients from Iran's registry and compare them with different reports throughout the world.

**Methods.** From a cohort of 7504 Iranian patients with Behçet's disease those diagnosed before the age of 16 years were included in this study. Data was collected on a standard protocol comprising 105 items, including demographic features, type of presentation, and different clinical and laboratory findings. A confidence interval (CI) at 95% for each item, and a standard deviation (SD) for the means was calculated. Comparisons were done by independent t or Mann-Whitney U, and chi-square tests. P-values less than 0.05 were considered statistically significant.

**Results.** PED-BD was seen in 2.7% of patients. The male/female ratio was 1.02/1, and the mean age at onset was 10.5 $\pm$ 3.4. Positive familial history for BD was present in 9.9% of patients, and for oral aphthosis (OA) in 46.3%. As a first manifestation, OA was the most frequent (75%) followed by ocular lesions in 19.1%, genital ulcers (GU) in 7.4% and joint involvement in 4.9%. The prevalence rates of various manifestations were as follows: OA: 91.7%; GU: 42.2%; skin: 51.5% (pseudofolliculitis: 43.1%, erythema nodosum: 10.3%); ocular lesions: 66.2% (anterior uveitis 52%, posterior uveitis 58.3%, retinal vasculitis 39.7%); articular manifestations: 30.9%; neurological involvement: 4.9%; vascular involvement: 6.4% (venous 4.9%, arterial 2.5%); gastrointestinal manifestations: 5.9%; epididymo-orchitis: 8.7% (boys). The laboratory findings were as follows: High ESR ( $\geq 20$ ): 50.8%; abnormal urine: 14.1%; positive pathergy test: 57%; HLA-B5/51: 48.7%; and HLA-B27: 13.4%. ICBBD criteria has the highest sensitivity for the classification of PED-BD patients in Iran (91.7%).

**Conclusion.** The clinical spectrum of PED-BD in Iran in this study was similar to that of other reports; however, genital ulcers, skin lesions (notably erythema nodosum), and gastrointestinal involvement were noticed to occur less frequently, while ocular lesions were more frequent and more severe compared to other reports.

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Poster Session 2 - Oral Presentations

O08-P134

**Behçet's Uveitis: Comparison of Interferon- $\alpha$  vs. anti-TNF- $\alpha$  therapy in a clinical cohort**

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**Introduction.** International guidelines advocate the use of interferon- $\alpha$  (IFN) or anti-TNF- $\alpha$  (aTNF) in severe refractive posterior segment uveitis in Behçet's Disease (BD). No comparative trial between the 2 treatment modalities exists

**Aims.** Retrospective clinical cohort analysis comparing IFN and aTNF outcomes in uveitis

**Methods.** In 52 patients (100 eyes) with BD related uveitis attending the clinics of the Rotterdam Eye Hospital, retrospective analysis for visual acuity outcome and inflammatory activity was performed regarding the use of systemic treatment, use of IFN or aTNF.

**Results.** 57 eyes received local treatment or a combination of classic immunosuppressive systemic drugs including azathioprine during follow-up. 31 refractive eyes were treated (mainly) with aTNF (majority adalimumab, others infliximab), 12 refractive eyes were treated (mainly) with IFN. Average follow up was 14.3 $\pm$ 8.7 years (mean  $\pm$  SD). The classically treated group had a significantly better visual acuity at presentation (Snellen 0.6 $\pm$ 0.4,  $p=0.013$ ), and 10 years outcome (0.7 $\pm$ 0.4 Snellen) compared to the aTNF and IFN groups. In the IFN group, visual acuity at presentation and 10 years was 0.3 $\pm$ 0.4 Snellen and 0.5 $\pm$ 0.3 Snellen ( $p=0.01$ ) respectively. In the aTNF group visual acuity at presentation and 10 years was 0.5 $\pm$ 0.4 Snellen and 0.5 $\pm$ 0.4 ( $p=0.62$ ) respectively. There was no significant difference between the 10 years visual outcome in aTNF vs IFN groups ( $p=0.14$ ). Similarly, there was no significant difference in inflammatory episodes after start of IFN or aTNF therapy. 35% of aTNF treated eyes with BD used reduced administration intervals (eg Adalimumab weekly or every 10d instead of 2-weekly regimens).

**Conclusion.** Regarding long term visual acuity outcome or inflammatory activity in refractive BD related uveitis, we found no difference between aTNF or IFN therapy. Choice between drugs therefore mainly depends on clinician's experience, side effects, patient's choice and availability.

O09-P084

**Venous vessel wall thickness in lower extremity is increased in male Behçet's disease patients**

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**Introduction.** Vascular involvement is seen in up to 40% of the patients with Behçet's Disease (BD), especially in young males and is one of the major causes of mortality and morbidity. Lower extremity vein thrombosis due to vascular inflammation is the most frequent form of vascular involvement in BD. Recently, assessment of vessel wall thickness (VWT) and venous dilatation by US is suggested to be valuable in patients with vascular inflammation.

**Aims.** In this study, we investigated whether vessel wall thickness or dilatation is present in young male BD patients prone to venous vascular disease.

**Methods.** Thirty male patients with BD without major organ involvement and 29 male patients with Vascular BD (VBD) followed in Marmara University Behçet's Clinics, 24 healthy male controls and 27 male patients with ankylosing spondylitis (AS) were included the study. Bilateral lower extremity venous doppler ultrasonography (US) was performed by an experienced radiologist blinded to cases. No patients except VBD were under immunosuppressive treatment. Bilateral common femoral vein (CFV) wall thickness and great/small saphenous vein dilatations were examined. Behçet Syndrome Activity Score (BSAS) was used for the general assessment of disease activity. In 10 patients, CFV wall thickness was measured by 2 different radiologist (RE, RA) in the same day to calculate "inter-observer reliability". Correlation between radiologists was good ( $r=0.765$ ,  $p<0.001$ ).

**Results.** Mean disease duration was 9.1 $\pm$ 6 years in patients with BD. BSAS score was 24 $\pm$ 17. All venous measurements were significantly higher in BD compared to AS and healthy controls ( $p<0.001$  for all, Table I). When we compared mucocutaneous BD (m-BD) vs VBD, all measurements of patients with VBD were higher than m-BD, however only left CFV thickness and width of right great saphenous vein reached statistical significance ( $p<0.001$ , and  $p=0.028$ , respectively). There were no correlations between BSAS, acute phase reactants and venous wall measurements.

**Conclusion.** In our study, an increased venous vessel wall thickness in lower extremity was shown in male BD patients with or without vascular involvement. As a similar change was not observed in control groups, increased VWT might be an early sign of venous inflammation in patients with BD rather than a result of non-specific systemic inflammation.

**Table I.** Venous wall measurements of lower extremity in study groups.

	Behçet's Disease (n=59)	Ankylosing Spondylitis (n=27)	Healthy Controls (n=28)	P Value
Age, years	32.5 (23-42)	32 (20-37)	31.5 (25-42)	0.23
Body Mass Index (kg/m <sup>2</sup> )	25.1 (18-33)	25 (18-32)	23.8 (20-29)	0.213
Right Common femoral VWT (mm)	0.8 (0.04-1.8)	0.3 (0.1-0.6)	0.25 (0.06-0.4)	<0.001
Left Common femoral VWT (mm)	0.8 (0.3-1.6)	0.3 (0.1-0.5)	0.2 (0.04-0.6)	<0.001
Right Great saphenous width (mm)	3.1 (0-6.4)	2.5 (1.1-3.5)	2.1 (1.3-3.5)	<0.001
Left Great saphenous width (mm)	3.1 (0-7.4)	2.6 (0.3-4.8)	2.4 (1.6-3.6)	<0.001
Right Small saphenous width (mm)	2.8 (0-5.3)	1.7 (1-3.1)	1.4 (0.9-3.7)	<0.001
Left Small saphenous width (mm)	2.7 (0-5.2)	1.8 (1.1-3.4)	1.6 (0.8-3.6)	<0.001
Left Great saphenous width (mm)	3.1 (0-7.4)	2.6 (0.3-4.8)	2.4 (1.6-3.6)	<0.001

VWT: Venous wall thickness

O10-P087

**The association of alpha-melanocyte stimulating hormone, vasoactive intestinal peptide with fatigue and quality of sleep in Behçet's disease**

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**Introduction.** Fatigue and disturbed sleep patterns are frequent symptoms in Behçet's Disease (BD). They have a major impact on patients' psychology, social well-being, disease activity and quality of life (QoL). This ultimately has a major impact on all aspects of normal living. To attempt to understand this, Artificial Intelligence (AI) was used to identify potential biomarkers. These were Alpha-melanocyte stimulating hormone ( $\alpha$ -MSH), vasoactive intestinal peptide (VIP) and some inflammatory cytokines.

**Aims.** This study was designed to investigate whether  $\alpha$ -MSH, VIP and inflammatory cytokines were similar in BD patients compared with healthy participants. Also, to scrutinise the association of these biological molecules with oral and genital ulceration activity as well as the Behçet's disease current activity form (BDCAF). The BD patients' prescribed medication was also assessed and correlated with the study outcomes.

**Methods.** A cohort of 127 participants, 97 BD patients and 30 healthy control (HC). All completed the Multi-Dimensional Assessment of Fatigue questionnaire (MAF) and the Pittsburgh Sleep Quality Index (PSQI) on the day of their clinical assessment. Enzyme-linked immunosorbent assays (ELISA) were used to evaluate the serum concentrations of  $\alpha$ -MSH, VIP and cytokines (IL-1 $\beta$ , IL-6, IL-10, and TNF- $\alpha$ ).

**Results.** 64% of BD patients experienced high fatigue scores, and 63% had poor quality of sleep. When BD and HC were compared the MAF and PSQI scores as well as the serum concentrations of  $\alpha$ -MSH, VIP, and IL-6 were significantly higher in BD (P values were: 0.001, 0.001, 0.001, 0.004 and 0.036, respectively). Both  $\alpha$ -MSH and IL-6 had significant impact on MAF and PSQI. Interestingly, VIP had a significant influence on PSQI and disease activity, but not on MAF.

**Conclusion.** A better understanding of these complex clinical and biochemical interactions between  $\alpha$ -MSH, VIP, and IL-6 might lead to the development of novel approaches to manage fatigue and sleep disorders as well as disease activity in BD patients.