Objectives: To evaluate the effects of the disease and its treatment on serum AMH levels for Behcet's disease (BD), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (SSD).

Methods: The study included 73 patients with RDs from 18 to 40 years: 42 patients with BD, 12 with SLE, 11 with RA, 8 with SSD, the control group consisted of 15 healthy women. Enzyme-linked immunosorbent assay (ELISA) was used to measure AMH levels. Parametric and nonparametric statistical methods of Statistica 8.0 package were used for statistical processing of data.

Results: Mean age in BD patients was 30.0 years, in SLE and RA -33.5 years, in SSD - 35.0 years, and 32.0 years in the control group. The average disease duration was 4.5 years, 11.5 years, 4.0 years and 6.0 years, respectively.

	BD, n=42	SLE, n=12	RA, n=11	SSD, n=8	Control, n=15
Mean age, years	30,0 [26;35]	33,5 [29;38]	33,5 [24;36]	35,0 [28;40]	32,0 [26;35]
Average disease duration, years	4,5 [2,6;9,0]	11,5 [2,8;18]	4,0 [4,0;6,0]	6,0 [2,0-10,0]	-
Mean AMH level, ng/ml	2,5 [1,1;3,7]	3,5 [0,4-7,1]	3,35 [2,0;7,6]	2,5 [0,3;7,1]	3,1 [1,9;5,4]

There were no significant differences in the mean AMH levels between the groups. No association between AMG levels and clinical manifestations, disease activity or duration of rheumatic disease was found. Baseline AMH – in treatment-naïve patients before initiation of any DMARDs was assessed in 11 BD patients. A significant ($p>0.05$) decrease of AMH levels was established in patients with high SLE activity treated with CP. Of notice, all examined patients were additionally receiving a GEED -Rituximab.

Conclusion: Decreased ovarian function was found in patients with high SLE activity treated with CP with Rituximab.

Disclosure of Interests: None declared

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AB0478 CORONARY ATHEROSCLEROSIS IN BEHCET'S DISEASE

R. Goloeva¹, Z. Alekberova¹, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Behcet's disease (BD) is systemic vasculitis, which affects all types and sizes of vessels. Increased carotid intima-media thickness (IMT) is parameter associated with subclinical atherosclerosis.

Objectives: To determine the prevalence of atherosclerosis in pts with BD.

Methods: 95 BD pts were evaluated and 45 healthy controls matched for age and gender.

IMT was assessed by high-resolution B-mode ultrasonography. Serum concentration of high-sensitivity C-reactive protein (hs CRP) was measured by immunonephelometric assay (BN-100 Analyzer; Dade Behring). Lipid profile evaluation included total cholesterol, TGs, HDL, LDL and atherogenic index.

Results: The male-to-female ratio was 3,7:1, the mean age of pts was 29.7 (23-35) yrs, the mean age at the disease onset - 19,9 (14-25) yrs, the mean disease duration - 9,6 (4-15) yrs.

	BD, %	Healthy, %	P
Arterial hypertension	22,1	13,3	ns
Smoked	29,5	24,4	ns
Diabetes mellitus	0	0	ns
Lipid abnormalities	76,8	64,4	ns
Total cholesterol	5,0 ±1,40	5,3 ±0,96	ns
TGs	0,91 ±0,65	0,90 ±0,68	ns
HDL	1,18 ±0,39	1,26 ±0,29	ns
LDL	3,40 ±1,46	3,47 ±0,90	ns
Hs CRP	2,42 ±21,0	0,3 ±0,63	<0,00
Mean IMT carotid artery	0,68 ±0,09	0,64 ±0,09	ns
IMT <0,5 mm	31,6	6,6	<0,00
IMT > 0,5-0,89 mm	49,5	86,6	ns
IMT - 0,9 – 1,2 mm	13,68	6,6	ns
IMT > 1,2mm (plaques)	5,7	0	ns

The mean carotid IMT in BD pts was similar with controls. In pts thinning IMT and concentration of hsCRP was significantly higher compared with controls.

IMT correlated with age of pts, concentration of total cholesterol, LDL and hsCRP but did not correlated with clinical manifestation and disease duration. Carotid atherosclerotic plaques were found in 5 pts with BD – mean age 40,0±8,1, who had traditional cardiovascular risk factors (high body mass index, hypertension) and received long time therapy with glucocorticoids.

Conclusion: Coronary atherosclerosis in BD pts was lower than what we expected. The thinning IMT may be one of the risk factors for aneurysm formation in pts with BD.

Disclosure of Interests: None declared

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AB0479 PREGNANCY OUTCOMES IN PATIENTS WITH RHEUMATIC DISEASES.

Z. Alekberova¹, R. Goloeva¹, A. Lila¹, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background:

Objectives: To evaluate pregnancy outcomes in patients with Behcet's disease (BD), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (SSD).

Methods: The study included 73 patients with rheumatic diseases (RDs) aged 18 to 40 years signing the informed consent form and completing dedicated thematic chart. The mean age of participants was 30.0 years - for BD patients; 33.5 years - for SLE, 33.5 – for RA; and 35.0 for SSD patients; mean disease duration was 4.5 years, 11.5 years 4.0 years and 6.0 years, respectively. 23 patients (11 BD patients, 5 SLE, 5 RA 5 and 2 SSD 2) out of 73 never had pregnancies, including 15 virgo patients and 4 patients who were planning pregnancy in the near future. 158 pregnancies in 50 patients with rheumatic diseases (31 BD patients, 7 SLE, 6 RA, and 6 SSD pts) were retrospectively analyzed.

Results: Outcomes of 159 pregnancies in RD patients were as follows: 95 (60%) on time births of full-term babies; 2 cases (1.2%) of early neonatal death in two BD females (premature deliveries at 28 and 32 gestational weeks of babies with signs of extreme prematurity who died 1 day after birth); 35 pregnancies were terminated before 10 weeks of gestation: 34 pregnancies (in 4 patients) - at the woman's request, 1-for medical reasons (rubella at 7 weeks of gestation). Totally 27 cases of adverse pregnancy outcomes were documented in 20 patients (40% of 50 patients): 19 cases (in 14 patients) of intrauterine deaths, one case of ectopic pregnancy, 8 cases (in 6 patients) of early miscarriages (at 5, 6 and 10 weeks of gestation).

There were no cases of antiphospholipid syndrome documented.

Pregnancy outcomes in RD patients

	BD, n=31	SLE, n=7	RA, n=6	SSD, n=6
Pregnancy, n	107	16	17	18
Childbirth, n	71	9	9	6
Medical abortion, n	20	2	3	10
Intrauterine deaths, n	12	4	4	0
Miscarriage, n	4	1	1	2

Out of total 95 babies born to RD patients, two had recurrent aphthous stomatitis (in 2 BD patients), and one had congenital glaucoma (born to a mother with neuro-Behcet's). 10 BD and 2 RA are patients multipara mothers who are raising 3 and more children.

Conclusion: Rheumatic diseases are associated with high incidence of adverse pregnancy outcomes.

Disclosure of Interests: None declared

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AB0480 AN OPEN-LABEL, EXPLORATORY STUDY TO ESTABLISH THE EFFICACY AND SAFETY OF 1-YEAR CANAKINUMAB TREATMENT IN BEHCET'S DISEASE PATIENTS WITH NEUROLOGIC OR VASCULAR INVOLVEMENT

A. Güllü¹, M. Kurtuncu¹, M. Erdugan¹, E. Oguz², T. Gunduz², G. Akman Demir², S. Sevgi³, S. Turgay⁴, E. Acar⁵. ¹Istanbul Faculty of Medicine, Istanbul, Turkey; ²Istanbul Faculty of Medicine, Istanbul, Turkey; ³Novartis Turkey, Istanbul, Turkey; ⁴Novartis Turkey, Istanbul, Turkey; ⁵Novartis Turkey, Istanbul, Turkey

Background: Previous observations in Behcet's disease (BD) patients receiving anti-IL 1 therapies suggested that dosage and route of administration may be critical in controlling disease manifestations. This was supported by favorable observations with infliximab infusions reaching higher serum trough levels in refractory BD patients compared to other anti-TNF agents.

Objectives: The primary objective was to evaluate the safety and efficacy of intravenous (IV) canakinumab (CAN) on the clinical and inflammatory findings of BD patients with neurologic and vascular involvement.

Methods: Biologic-naïve BD patients, who had a recent attack of large vessel vascular or parenchymal neurologic disease within the last month were enrolled and all received 300mg CAN IV without a change in other medications. Response was assessed on day 30 as the primary objective; partial

responders were able to take the 2nd 300 mg IV on day 30 and continued the treatment with monthly 150 mg IV 4 times. Others continued the treatment with 150 mg IV monthly. At month 6, patients were able to switch to SC injections or continue 150 mg IV for 6 months. Non-responder patients were dropped out. Prednisolone dosage was ≤ 20 mg at baseline and not increased during the trial. Complete response was defined as full clinical recovery to pre-attack state, disappearance of MRI lesions, normalization of CSF findings; partial response was defined as partial improvement in clinical findings, which were still worse than pre-attack state, with MRI lesions becoming smaller with no or less enhancement, and a decrease in CSF cell count. Complete response of vascular findings was defined as $\geq 50\%$ improvement in patient's and physician's global assessments, $\geq 50\%$ reduction in CRP; along with stable or $\geq 20\%$ reduced aneurysm size or stable or $\geq 20\%$ reduced calf swelling; and partial response was an improvement between 20-49% in global assessments, 20-49% reduction in CRP; stable or $\leq 20\%$ reduced aneurysm size or $\leq 20\%$ reduced calf swelling.

Results: 9 subjects were screened, and 8 male subjects (5 vascular, 3 neurologic) aged 27.3 ± 2.3 years entered the study. No new attack or worsening of manifestations was observed, and at least a partial response was obtained in all patients on day 30. Two vascular patients (2/5, 40%) and 1 neurologic patient (1/3, 33%) received another 300 mg infusion on day 30; one of them left the study on day 120 because of safety concerns after noticing the use of illicit drugs, and the other required 150 mg IV CAN after day 180 and discontinued the study because of the worsening of pulmonary artery aneurysm, despite favorable response in venous findings. The remaining 3 patients (3/5, 60%) with deep vein thrombosis completed the study with clinical and radiological improvement. 2 patients with parenchymal involvement had lesions in the brain stem and showed complete improvement of clinical findings between 1-3 months and radiologic findings between 3-6 months. Clinical findings of 1 patient with sinus thrombosis improved within 2 months, and the last cranial MRI showed that the vein thrombus was recanalized. Patients experienced other mild manifestations of BD following a switch to SC administration.

Conclusion: Response to CAN without high-dose methylprednisolone treatment suggests that IL-1 antagonism plays a role in acute exacerbations of neurologic and vascular manifestations of BD, and no new safety signal was recorded with IV use. Favorable responses during the early months of the study and development of clinical and laboratory findings after switching to SC administration may suggest that achievement of higher serum trough levels may be critical, and up-titration of the dosages may provide better results in individual patients with higher inflammatory activity.

References: NA

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AB0481

EFFICACY OF APREMILAST FOR THE TREATMENT OF GENITAL ULCERS ASSOCIATED WITH ACTIVE BEHÇET'S SYNDROME: A COMBINED ANALYSIS OF TWO RANDOMIZED CONTROLLED TRIALS

G. Hatemi¹, A. Mahr², M. Takeno³, D. Kim⁴, M. Melikoglu¹, S. Cheng⁵, S. Mccue⁵, S. Richter⁵, M. Brunori⁵, M. Paris⁵, M. Chen⁵, Y. Yazici⁶. ¹Istanbul University-Cerrahpaşa, Cerrahpaşa Medical School and Behçet's Disease Research Center, Istanbul, Turkey; ²Cantonal Hospital St. Gallen, St. Gallen, Switzerland; ³Nippon Medical School, Graduate School of Medicine, Tokyo, Japan; ⁴Yonsei University College of Medicine and Severance Hospital, Seoul, Korea, Rep. of (South Korea); ⁵Amgen Inc., Thousand Oaks, United States of America; ⁶New York University School of Medicine, New York, United States of America

Background: Behçet's syndrome is a chronic, multi-system inflammatory disorder characterized by painful, recurrent oral ulcers (OU) and genital ulcers (GU).¹ The GU associated with Behçet's syndrome can contribute to difficulties with sexual activity, walking, and sitting²; may cause scarring¹; and may impair quality of life.^{1,2} Apremilast (APR), an oral phosphodiesterase 4 inhibitor, has demonstrated efficacy in the treatment of the OU associated with Behçet's syndrome in the phase III, randomized RELIEF study (BCT-002).³

Objectives: To describe the efficacy of APR for the treatment of GU associated with active Behçet's syndrome in the RELIEF study and in a pooled data analysis of RELIEF and the phase II study.

Figure 1. Complete Response of GU at Week 12 in Patients With GU at Baseline (Pooled RELIEF and Phase II Study Data)

*P=0.011. GU=genital ulcer.

Methods: Adult patients (≥ 18 years of age) with active Behçet's syndrome and ≥ 3 OU at randomization or ≥ 2 OU at screening and randomization, without active major organ involvement, were randomized (1:1) to APR 30 mg twice daily or placebo (PBO). In RELIEF, clinical improvement in GU was assessed by evaluating the time to the first GU recurrence after loss of complete response, the mean number of GU in patients without GU at baseline, and the proportion of patients who were GU-free (complete response) at Week 12 (regardless of baseline GU status). A pooled analysis of patients in RELIEF and a randomized, phase II study⁴ were conducted to assess achievement of GU complete response in patients with GU at baseline. In patients with GU complete response before Week 12, the median time to the first GU recurrence after loss of complete response was based on Kaplan-Meier estimates. The mean number of GU was summarized descriptively using data as observed. Between-group differences in the proportion of patients who were GU-free at Week 12 were analyzed by Cochran-Mantel-Haenszel test using non-responder imputation to handle missing data. Statistical tests were 2 sided ($\alpha=0.05$).

Results: A total of 207 patients were randomized and received ≥ 1 dose of study medication (APR: n=104; PBO: n=103). In all, 17 patients in the APR group and 17 in the PBO group had GU at baseline, with mean GU counts of 2.9 (APR) and 2.6 (PBO). Among patients with GU at baseline in RELIEF, 12/17 (70.6% [APR]) and 7/17 (41.2% [PBO]) achieved GU complete response at Week 12 ($P=0.110$). The median time to first GU recurrence in these patients occurred earlier with PBO (6.1 weeks) vs. APR (not calculable). In the pooled analysis of RELIEF and the phase II study, a significantly greater proportion of patients with GU at baseline achieved GU complete response at Week 12 with APR vs. PBO (21/27 [77.8%] vs. 9/23 [39.1%]; $P=0.011$) (Figure 1). The proportion of patients who were GU-free was significantly greater with APR (92/104 [88.5%]) vs. PBO (72/101 [71.3%]), regardless of baseline number of GU ($P=0.002$) (Figure 2).

Conclusion: The number of patients with GU was low, but the totality of the data shows a favorable trend in the treatment effect of APR on GU. Greater proportions of APR-treated patients were GU-free at Week 12 vs. patients receiving PBO, and the time to the first GU recurrence occurred earlier with PBO vs. APR.

References:

- Kokturk A. Patholog Res Int. 2012;2012:690390.
- Senusi A, et al. Orphanet J Rare Dis. 2015;10:117.
- Hatemi G, et al. N Engl J Med. 2019;381:1918-1928.
- Hatemi G, et al. N Engl J Med. 2015;372:1510-1518.

Figure 2. Complete Response of GU at Week 12* in Patients Regardless of the Number of GU at Baseline

*In the RELIEF study. *P=0.002. GU=genital ulcer.