OP0058

CARDIOVASCULAR AND CEREBROVASCULAR RISK IN PATIENTS WITH SMALL VESSEL VASCULITIDES: A COMPARATIVE ANALYSIS BETWEEN AORTIC STIFFNESS, CAROTID SONOGRAPHY AND SCORE

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Background: Cardiovascular (CV) and cerebrovascular (CVB) risk have not been adequately examined in the setting of patients with small vessel vasculitides. In particular, data on CV/CVB surrogate markers are scarce and the diagnostic value of traditional CV risk scores, such as the Systematic Coronary Risk Evaluation (SCORE) and its EULAR modified version (mSCORE) is unknown.

Objectives: Aims of this study were to examine gold standard surrogates of CV risk and subclinical atherosclerosis (1), as well as novel duplex-sonographic markers of CVB risk in a cohort of patients with small vessel vasculitides. Moreover, we sought to evaluate for the first time the diagnostic value of SCORE and mSCORE in identifying patients at high CV and CVB risk.

Methods: SCORE/mSCORE and the gold standard marker of aortic stiffness (carotid-femoral pulse wave velocity; cFPWV) were examined in patients with small vessel vasculitides and healthy controls across 3 Rheumatology Centers. Moreover, sonography of the common- (CCA), internal- (ICA) and external- (ECA) carotid arteries was performed in subsets of both groups, evaluating carotid intima-media-thickness (cIMT), plaque presence and duplex-sonographic indices of CVB risk, such as the resistance- (RI) and pulsatility-index (PI). Disease characteristics, clinical and serological activity markers, as well as traditional CV risk factors were also documented.

Results: We recruited 46 patients with small vessel vasculitides [granulomatosis with polyangiitis (n=33), eosinophilic granulomatosis with polyangiitis (n=6), microscopic polyangiitis (n=4), cryoglobulinemic vasculitis (n=1), urticaria vasculitis (n=2): 76.1% female, median age 61.5 years (52-72.25, IQR)] and 105 healthy controls [76.1% female, median age 61.5 years (52-72.25, IQR)]. cFPWV was significantly higher in the patient group compared to the control group, even after statistical corrections for confounding factors (i.e. age, gender: different in the two groups) (8.4 m/s vs. 6.8 m/s; $p_{adj} < 0.001$). Moreover, carotid sonography revealed higher CVB surrogates in the patient subgroup, compared to controls. According to SCORE and (EULAR)-mSCORE, 0.9% and 15.8% of the patients had high CV risk (defined as SCORE/mSCORE >5), respectively. However, cFPWV revealed an increased CV risk in 28.2% of the patients. Moreover, carotid sonography showed signs of subclinical carotid arteriosclerosis in 50% (plaques) and 71.7% (cIMT >0.9mm) of the patients, respectively.

Conclusion: Herein, we could show that patients with small vessel vasculitides had higher aortic stiffness and subclinical carotid atherosclerosis, compared to controls and could thus have higher CV and CVB risk. Moreover, we were able to demonstrate for the first time that SCORE/mSCORE performed poorly in identifying patients at high CV risk and carotid atherosclerosis compared to cFPWV and carotid sonography respectively. Thus, cFPWV and carotid sonography could improve CV and CVB screening in patients with small vessel vasculitides.

Table 1. Descriptive characteristics.

	Controls (n=105)	Patients (n=46)	Significance (p)
cFPWV† (m/s)	6.80 (6.05-7.5)	8.40 (7.26-10.66)	<0.001*
Age† (years)	50 (39.50-56.5)	61.50 (52-72.25)	<0.001*
Gender (female)	95 (90.5%)	35 (76.1%)	0.019*
Nicotin (smokers)	21 (20%)	5 (11.1%)	0.190
Antihypertensive drugs	18 (17.1%)	27 (65.9%)	<0.001*
BMI†	23.73 (21.1-27.1)	25.14 (22.81-28.70)	0.074
Mean art. pressure‡	93.45±10.68	96.19±10.68	0.150
ESR† (mm/h)	-	20.00 (11-41.5)	-
ANCA	-	25 (54.3%)	-
Creatinine†	0.77 (0.72-0.81)	0.94 (0.8-1.31)	<0.001*
Cholesterol‡ (mg/dL)	-	216.88±40.16	-
Prednisolone† (mg)	-	5.63 (1.75-16.38)	-
Lung involvement	-	17 (37%)	-
Kidney involvement	-	17 (37%)	-
Ear-nose-throat (ENT)	-	16 (34.8%)	-

†median (IQR); ‡mean±standard deviation; *t test; *p<0.05

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OP0059

MAVRILIMUMAB (ANTI GM-CSF RECEPTOR A MONOCLONAL ANTIBODY) REDUCES RISK OF FLARE AND INCREASES SUSTAINED REMISSION IN A PHASE 2 TRIAL OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: T helper (Th)1 and Th17 lymphocytes play a role in the pathogenesis of giant cell arteritis (GCA). Current treatments primarily target the Th17 axis, possibly leaving residual Th1 activity. Granulocyte macrophage colony stimulating factor (GM-CSF), a mediator of Th1 and Th17 cells, is a pathogenic factor in GCA.

Objectives: To evaluate the efficacy and safety of the GM-CSF inhibitor mavrilimumab in patients with GCA.

Methods: Randomized, double-blind, placebo-controlled phase 2 trial enrolling patients with active, biopsy- or imaging-proven new onset (N/O) or relapsing refractory (R/R) GCA. Active disease: GCA symptoms and erythrocyte sedimentation rate (ESR) (>30mm/hr) and/or C-reactive protein (CRP) (≥1 mg/dL) elevation within 6 weeks from randomization. Corticosteroid-induced remission (resolution of GCA symptoms and CRP <1 mg/dL or ESR <20mm/hr) was required by baseline. 3:2 randomization to mavrilimumab 150mg or placebo subcutaneously every 2 weeks and protocol-defined 26-week prednisone taper starting at 20-60 mg/day. Primary efficacy endpoint: time to first adjudicated flare (ESR ≥30mm/hr and/or CRP ≥1 mg/dL and GCA symptoms or new/worsening vasculitis on imaging) by Week 26 in all treated patients. Key secondary endpoint: sustained remission through Week 26. Safety up to Week 38 was assessed.

Results: 70 patients (35 N/O, 35 R/R) were enrolled (mavrilimumab [N=42] or placebo [N=28]). Mean (SD) age was 69.7 (7.48) years and 71.4% were female. Flare by Week 26 occurred in 8 (19%) and 13 (46.4%) patients receiving mavrilimumab and placebo, respectively (27.4 percentage points reduction). Median time to flare by Week 26 could not be estimated in the mavrilimumab group due to too few events (Not Estimable) and was 25.1 weeks [95% CI: (16.0, NE)] in the placebo group (HR [95% CI] 0.38 [0.15, 0.92]; p=0.0263) (Figure). Sustained remission at Week 26 occurred in 83.2% of patients receiving mavrilimumab and 49.9% of those receiving placebo (33.4 percentage points increase; p=0.0038). Results were consistent across disease type subgroups (HR for flare: N/O 0.29 [95% CI: 0.06, 1.31; nominal p= 0.0873]; R/R 0.43 [95% CI: 0.14, 1.30]; nominal p=0.1231), although not powered for significance (Table). Adverse events (AEs), mostly mild to moderate, were comparable between groups. There were 5 serious AEs (mavrilimumab 2 [4.8%], placebo 3 [10.7%]), none drug-related. No deaths or vision loss occurred. No adjudicated cases of pulmonary alveolar proteinosis were observed.

Figure 1. Time to Flare by Week 26 after randomization in All Patients.

Conclusion: Mavrilimumab was superior to placebo on the primary and secondary efficacy endpoints of time to flare and sustained remission at week 26 in patients with GCA. Mavrilimumab was well tolerated, and no new safety signals were observed.

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