FRI0262

CLINICAL OUTCOMES OF PATIENTS WITH GIANT CELL ARTERITIS WITH POLYMYALGIA SYMPTOMS ONLY VS CRANIAL SYMPTOMS ONLY TREATED WITH TOCILIZUMAB OR PLACEBO IN THE GIACTA TRIAL

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Background: GiACTA, a randomized, double-blind, placebo (PBO)-controlled study, demonstrated the efficacy and safety of tocilizumab (TCZ) in patients with giant cell arteritis (GCA).¹ Growing evidence has shown that TCZ is also effective for the treatment of polymyalgia rheumatica (PMR); however, data on this are limited.^{2,3}

Objectives: To evaluate the efficacy of TCZ in patients with GCA presenting with cranial symptoms only or PMR symptoms only in GiACTA.

Methods: GiACTA randomized 251 GCA patients to receive weekly or every other week TCZ plus a 26-week prednisone taper (TCZ + prednisone) or PBO plus a 26- or 52-week prednisone taper (PBO + prednisone).¹ In this post hoc analysis, baseline characteristics, sustained remission rate, number of flares, annual flare rate, time to flare, cumulative prednisone dose and safety were assessed in patients with PMR symptoms only and patients with cranial symptoms only at diagnosis. Disease flare was defined as the recurrence of signs or symptoms of GCA (including PMR) or an elevation in erythrocyte sedimentation rate attributable to GCA.

Results: Of 146 patients included in the analysis, 52 had PMR symptoms only and 94 had cranial symptoms only at diagnosis. Demographics and other patient characteristics are shown in **Table 1**. The hazard ratios for flare in patients receiving TCZ vs PBO were 0.77 (95% CI, 0.26-2.32) for patients with PMR symptoms only and 0.37 (95% CI, 0.13-1.01) for patients with cranial symptoms only. Of patients with PMR symptoms only, 18 flares occurred in 13/31 patients (41.9%) in the TCZ group and 20 flares occurred in 12/21 patients (57.1%) in the PBO group. Of patients with cranial symptoms only, 19 flares occurred in 12/58 patients (20.7%) in the TCZ group and 25 flares occurred in 17/36 patients (47.2%) in the PBO group (**Table 2**). For both the PMR and cranial symptoms only groups, annual flare rates were lower in patients receiving TCZ compared with those receiving PBO. The occurrence of adverse events and serious adverse events was similar between groups (**Table 2**).

Conclusion: TCZ improved clinical outcomes in patients who presented with PMR symptoms only or cranial symptoms only at diagnosis as indicated by a reduced incidence of flares. These findings suggest that TCZ is effective in patients with GCA with PMR or cranial symptoms.

REFERENCES:

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Table 1. Patient Characteristics and Treatment at Study Baseline

	PMR Symptoms Only at Diagnosis (n = 52)	Cranial Symptoms Only at Diagnosis (n = 94)
Age, mean (SD), y	64.5 (8.3)	70.8 (7.8)
Female, n (%)	39 (75.0)	64 (68.1)
White, n (%)	51 (98.1)	91 (96.8)
Weight, mean (SD), kg	70.06 (14.09)	71.78 (16.10)
Body mass index, mean (SD), kg/m ²	24.81 (3.95)	26.36 (5.44)
GCA diagnosis, n (%)		
Newly diagnosed	27 (51.9)	41 (43.6)
Relapsing	25 (48.1)	53 (56.4)
Disease duration, mean (SD), days	327.04 (600.89)	239.05 (404.94)
ESR, mean (SD), mm/h	24.98 (20.21)	24.56 (19.92)
CRP, mean (SD), mg/L	6.51 (9.44)	7.73 (12.70)
Diagnosis, n (%) ^a		
Positive temporal artery biopsy	9/12 (75)	72/79 (91.1)
Positive imaging	44/52 (84.6)	31/94 (33.0)
Prednisone dose, n (%)		
≤ 30 mg/d	27 (51.9)	53 (56.4)
> 30 mg/d	25 (48.1)	41 (43.6)
Treatment group, n (%)		
TCZ [†]	31 (59.6)	58 (61.7)
Placebo [‡]	21 (40.4)	36 (38.3)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; TCZ, tocilizumab.

^a Of patients with available results.

[†] TCZ 162 mg weekly or every other week with a 26-week prednisone taper.

[‡] Placebo with a 26- or 52-week prednisone taper.

Table 2. Clinical and Safety Outcomes

	TCZ [†] (n = 52)	Placebo [‡] (n = 94)	TCZ [†] (n = 58)	Placebo [‡] (n = 36)
Patients with ≥ 1 flare, n (%)	13 (41.9)	12 (57.1)	12 (20.7)	17 (47.2)
Patients with PMR symptoms, n (%)	8/13 (61.5)	7/12 (58.3)	7/12 (58.3)	8/17 (47.1)
Patients with cranial symptoms, n (%)	10/13 (76.9)	6/12 (50.0)	10/12 (83.3)	10/17 (58.8)
No. of flares	18	20	19	25
Patients with PMR symptoms, n (%)	10/18 (55.6)	10/20 (50.0)	7/19 (36.8)	11/25 (44.0)
Patients with cranial symptoms, n (%)	12/18 (66.7)	8/20 (40.0)	15/19 (78.9)	11/25 (44.0)
Annual flare rate, mean (SD) ^b	0.44 (0.85)	0.95 (1.24)	0.40 (0.83)	0.89 (1.81)
Patients with flare following remission, n (%)	11 (35.5)	11 (52.4)	11 (19.0)	10 (44.4)
Cumulative prednisone dose, prednisone, mg	1862.0	3671.5	1842.0	2965.5
Patients with ≥ 1 AE, n (%) ^c	30 (96.8)	20 (95.2)	55 (94.8)	30 (100)
Patients with ≥ 1 SAE, n (%) ^d	5 (16.1)	3 (14.3)	10 (17.2)	12 (33.3)

AE, adverse event; SAE, serious adverse event; TCZ, tocilizumab.

^a TCZ 162 mg weekly or every other week with a 26-week prednisone taper.

^b Placebo with a 26-week or 52-week prednisone taper.

^c Adverse event rate is calculated as the number of flares between the first clinical assessment of GCA and the first clinical assessment prior to entry into Part 2, divided by the time period between the 2 days, multiplied by 365.25.

^d Multiple occurrences of AEs are included. Denominators are all AEs in AEs.

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FRI0263

GRANULOMATOSIS WITH POLYANGIITIS (GPA): CARDIOVASCULAR MORBIDITY AND MORTALITY IN A POPULATION-BASED COHORT. A DANISH REGISTER STUDY

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Background: In order to understand and ultimately prevent cardiovascular (CV) morbidity and mortality in systemic inflammatory disorders we studied the epidemiology of CV disease in ANCA associated Vasculitis (AAV). There is growing evidence that both premature and pronounced atherosclerosis is associated with ANCA associated vasculitis (AAV) ¹⁻³. However, the exact mechanisms for CV involvement are unknown and probably multiple.

Objectives: To investigate if CV related comorbidity and death were increased among Danish AAV patients registered with a diagnosis of granulomatosis with polyangiitis (GPA) in Denmark.

To investigate if there was a temporal relation between diagnosis of GPA and CV disease and death.

Methods: A population-based cohort study was performed using the Danish Civil Registration System, the Danish National Patient Registry (all in-patient and out-patient contacts are registered with ICD diagnosis since 1995) and the Danish Cause of Death Register. Patients registered twice or more with a diagnosis of GPA (ICD8: 446.29 and ICD10: M313) during 1995-2016 were included. Annual incidence rate (IR), point prevalence (PP) and standardized mortality rate (SMR) were calculated. The entire adult population in Denmark served as control population. CV morbidity was divided into heart failure (HF) (ICD-10 code I42, I50, J81 and I110) and myocardial infarction (MI) (ICD-10 code I21-25). Death caused by CV disease (ICD-10 code I1-999) was registered.

Results: We identified 1829 individuals with GPA. The median annual IR was 20.5/1,000,000 and PP was 277/1,000,000 in 2015. Overall SMR was 2.14.

Among patients with GPA 171 had a hospital diagnosis of MI. Compared to the control population, the hazard ratio (HR) of MI was 2.47 (95% CI 1.45-4.55) during the first 3 months after the GPA diagnosis. From 3 months to one year declining to 1.41 (95%CI 0.80-2.49) and after 10 years the HR was still slightly increased to 1.64 (95%CI 1.20-2.23). The risk of a diagnosis of HF was markedly increased with a HR at 7.22 (95% CI 4.55-11.46) during the first 3 months after a GPA diagnosis, after three months up to one year 2.94 (95%CI 1.87-4.69), and 2.07 (95% CI 1.54-2.78) after 10 years.

The total number of CV deaths in the GPA cohort was 307. During the first three months after a GPA diagnosis, the HR was increased to 9.51 (95%CI 7.12-12.70) declining to 2.51 (95% CI 1.77-3.58) after one year, but still increased to 1.56 (95% CI 1.23-1.98) after 10 years.