Outcomes of giant cell arteritis patients treated with tocilizumab in a single neuro-ophthalmology practice

Giant cell arteritis (GCA) is a severe granulomatous occlusive vasculitis affecting medium to large arteries of the head and neck.[1] GCA can cause intense myointimal proliferation and vessel occlusion of the ophthalmic artery, central retinal artery, and short posterior ciliary arteries leading to irreversible vision loss.[2,3] Steroids remain the mainstay of treatment but usually require a slow taper over 1–3 years and lead to significant side effects in >80% of patients.[4] The Trial of Tocilizumab in Giant Cell Arteritis (GiACTA) in 2017 demonstrated the effectiveness of the recombinant monoclonal antibody interleukin-6 inhibitor tocilizumab (TCZ) combined with accelerated prednisone taper in achieving sustained glucocorticoid-free remission in GCA patients.[5] The purpose of our retrospective study was to compare outcomes of GCA patients treated with steroids alone versus patients treated with steroids and adjunctive tocilizumab in a single neuro-ophthalmology practice, as well as to compare outcomes from real-world practice with the outcomes reported from the prospectively designed GiACTA.

The study protocol was approved by the University of Oklahoma Health Sciences Center Institutional Review Board (IRB) and adhered to the tenets of the Declaration of Helsinki. We identified all biopsy-proven GCA patients managed by a single neuro-ophthalmologist (A.D.P.) from 2005 to 2022 and queried the medical records for cumulative steroid exposure (milligrams of prednisone), including planned taper and escape dosing necessary to maintain disease quiescence, and TCZ use. This provider's practice pattern includes initiating oral prednisone 1 mg/kg per day with tapering by 10 mg/month for steroid-only patients and tapering by 10 mg every 2 weeks for patients approved for concurrent subcutaneous TCZ 162 mg/0.9 mL weekly or biweekly. Length of steroid therapy (in months) required to achieve disease remission (cessation of prednisone or indefinite daily 1 mg dose), disease recurrence, defined by the return of GCA symptoms or new ocular ischemia; adverse events requiring medical intervention; and ocular ischemic complications at presentation (i.e., ischemic optic neuropathy, retinal/ophthalmic artery occlusion, ophthalmoplegia, or transient monocular vision loss) also were recorded. Excluded were patients lost to follow-up prior to 3 months of planned treatment, patients whose steroid dosing was not managed primarily by us, and patients with insufficient documentation.

A demographic and clinical summary of the 79 patients meeting study criteria appears in Table 1. Outcome measures of patients treated with steroid therapy alone versus patients treated with steroids and adjunctive TCZ appear in Table 2. There was a statistically significant reduction in mean cumulative steroid dose and length of steroid therapy, and outcomes of the TCZ group were not inferior to those of the steroid-only group regarding disease recurrence and adverse events requiring medical intervention—most frequently, hyperglycemia and infection/sepsis. However, we did not record mild or chronic adverse effects that were more difficult to quantify, such as insomnia, weight gain, fatigue, and quality-of-life indicators.

Notably, TCZ profoundly suppresses C-reactive protein and erythrocyte sedimentation rate independent of disease activity[6]; therefore, disease recurrence was defined as the return of previously resolved cranial (e.g., jaw claudication, temporal headache, and scalp tenderness) or polymyalgia rheumatica symptoms as opposed to elevation of acute-phase reactants.

GiACTA has primarily guided the use of TCZ for GCA, but several criticisms of this study should be considered in real-world practice, as demonstrated by our study. First, GiACTA used much more rapid, unconventional 26- and 52-week steroid tapering protocols (in turn, much lower cumulative steroid exposure) than those commonly encountered in real-world practice. Second, only 0.8% of GiACTA participants had ischemic optic neuropathy (ION)[7]; 44.3% of our study population presented with ION, and 70.9% presented with ocular ischemia of any kind, suggesting that the GiACTA population was comprised of patients with milder forms of disease. Our study, as well as that of Hayreh et al.,[8] suggests that patients with severe forms of GCA present to neuro-ophthalmologists, and our study demonstrates that these patients require much higher cumulative steroid exposure than those encountered in GiACTA (nearly a fourfold increase in both steroid-only and TCZ groups). Therefore,

Table 1—Demographic and clinical characteristics of the study population

Characteristic	Steroids only (n = 49)	Steroids + TCZ (n = 30)	*p* Value	Test
Age, mean, (SD; range)	76.6 (7.6; 60–95)	74.1 (8.8; 58–92)	0.094	*t* Test
Sex				
Female, % (n)	67.3 (33)	60.0 (18)	0.629	Fisher's exact test
Male, % (n)	32.7 (16)	40.0 (12)		
Ocular manifestations of GCA, % (n)	69.4 (34)	73.3 (22)	0.805	Fisher's exact test

TCZ, tocilizumab; GCA, giant cell arteritis

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Table 2—Comparison of outcome measures of patients treated with steroid therapy alone versus patients treated with steroids and adjunctive TCZ

Characteristic	Steroids only (n = 49)	Steroids + TCZ (n = 30)	*p* Value	Test
Cumulative steroid exposure, mean mg of prednisone (SD)	11,139.5 (6257.5)	8263.6 (4263.2)	0.015	*t* Test
Length of steroid therapy, months (SD)	26.5 (31.9)	14.8.0 (11.6)	0.029	*t* Test
Disease recurrence by GCA symptoms or ocular ischemia, % (n)	24.5 (12)	23.3 (7)	0.609	Fisher's exact test
Adverse events requiring medical intervention, % (n)				
Any	—	53.3 (16)	0.647	Fisher's exact test
Sepsis/infection	16.3 (8)	20.0 (6)		
Hyperglycemia or diabetic ketoacidosis	10.2 (5)	20.0 (6)		
Musculoskeletal (osteoporosis, osteopenia, avascular hip necrosis, spinal compression fracture)	4.1 (2)	6.7 (2)		
Uncontrolled hypertension	4.1 (2)	0		
Gastrointestinal (melena, ulcer, or perforation)	2.0 (1)	0		
Mean follow-up time, months (SD)	51.7 (47.4)	29.2 (17.9)	0.0083	*t* Test

TCZ, tocilizumab; GCA, giant cell arteritis

adjunctive TCZ should be strongly considered to reduce cumulative steroid exposure in these patients.

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Footnotes and Disclosure

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