What to do when you suspect GCA

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28TH JULY 2019

Ethnicity

Ethnicity is a major risk factor

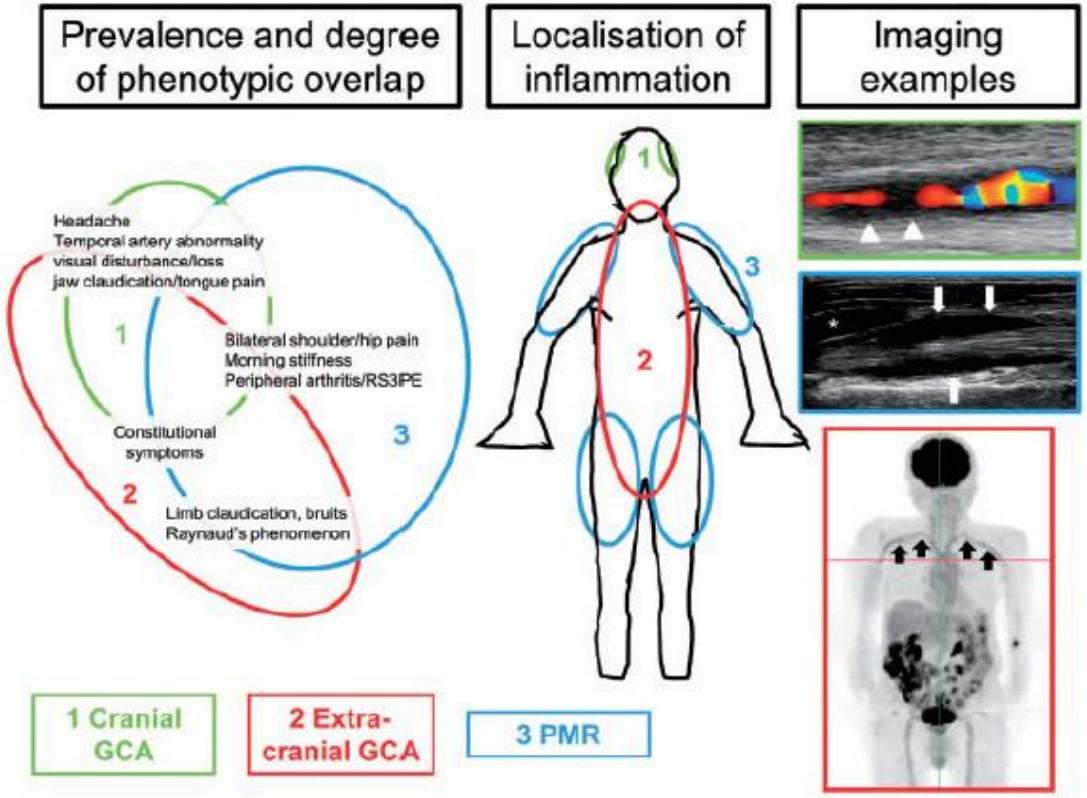
Highest incidence in Scandinavian countries and Americans of Scandinavian descent 17 per 100000

In southern Europe and Mediterranean countries incidence rates are lower less than 10 per 100000

GCA is unusual in Latinos, Asians and Arabs

Decidedly uncommon if African Americans

Phenotypes of Disease



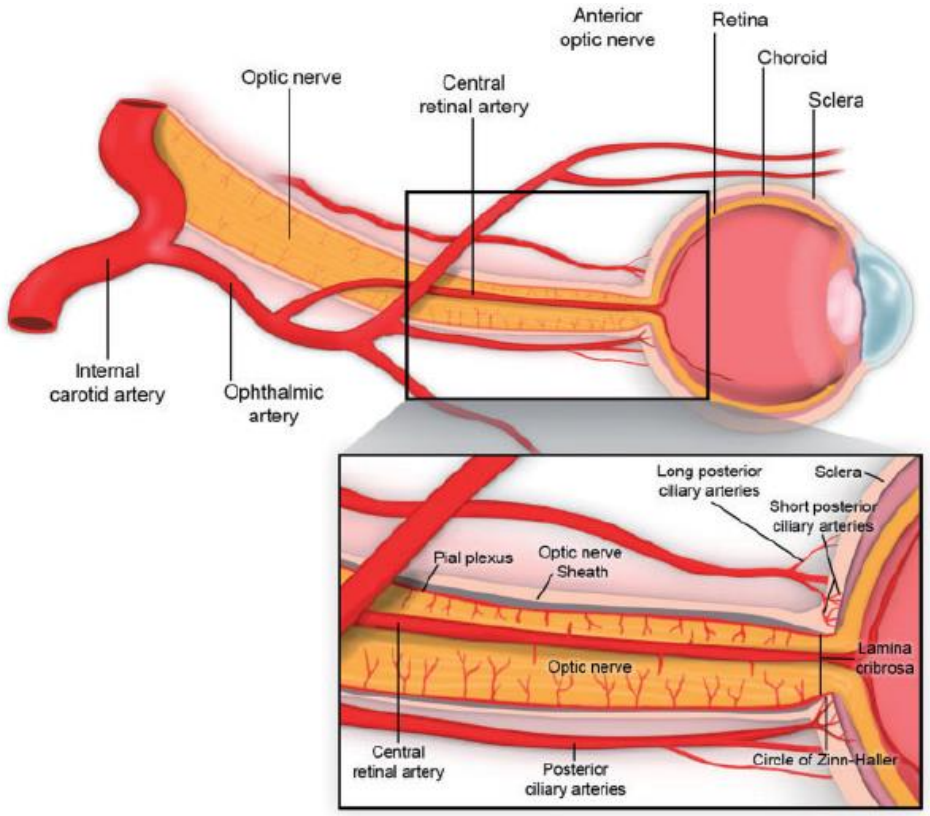
Symptoms and signs

Symptoms and signs	Cranial GCA	LV-GCA	PMR
Headache	++	–	–
Arterial swelling/tenderness, bruits	+	+	–
Jaw claudication/tongue pain	++	–	–
Visual symptoms/complications	++	–	–
Fever, weight loss	+	++	++
Arm claudication, RP	+	++	–
Polymyalgic symptoms	+	++	++
Acute phase reactants	++	++	++
Peripheral arthritis/RS3PE syndrome	+	+	++

Diagnosis

Original criteria	Suggested expansion
Age at disease onset ⩾50 years	Age at disease onset ⩾50 years
New onset headache of or new type of localized pain in the head	Any of the following: New onset headache of new type of localized pain in the head, **Visual symptoms, sight loss, PMR, Constitutional symptoms, Jaw and/or tongue claudication**
Abnormality of temporal artery (tenderness to palpation or decreased pulsation unrelated to arteriosclerosis)	Abnormality of temporal **and/or extra-cranial arteries** (tenderness to palpation or decreased pulsation, **bruits of extra-cranial arteries** unrelated to arteriosclerosis)
ESR ⩾50 mm/h	ESR ⩾50 mm/h and/or **CRP levels ⩾10 mg/l**
Abnormal artery biopsy	Abnormal artery biopsy and/or **abnormal imaging result (US, MRI and/or ^{18}F-FDG PET)**[a]

Blood supply



(Hayreh, S.S. 1974)

PATHOGENESIS

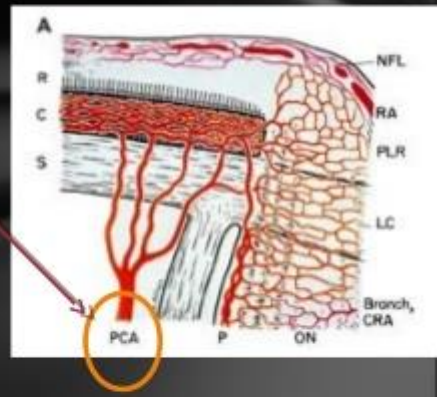
- In the eye, GCA has a special predilection to involve the posterior ciliary artery, resulting in its thrombotic occlusion, cause the development of AAION and visual loss.

Posterior ciliary artery is the main source of blood supply to the optic nerve head

Occlusion of the posterior ciliary artery results in infarction of a segment or the entire optic nerve head

Depending upon the area of the optic nerve head supplied by the occluded posterior ciliary artery

Results in development of A-AION and in massive visual loss.



LV - GCA

Stronger female predominance

Younger age of onset

Longer time to diagnosis

Lower inflammatory markers

LV- GCA clinical sign

Limb claudication

Vascular bruit

Pulse discrepancies

Aortic regurgiatation

Clinical examination at a minimum

Both upper limb BP

Cardiac auscultation

Vascular bruits and abnormal pulse in carotid and limb arteries

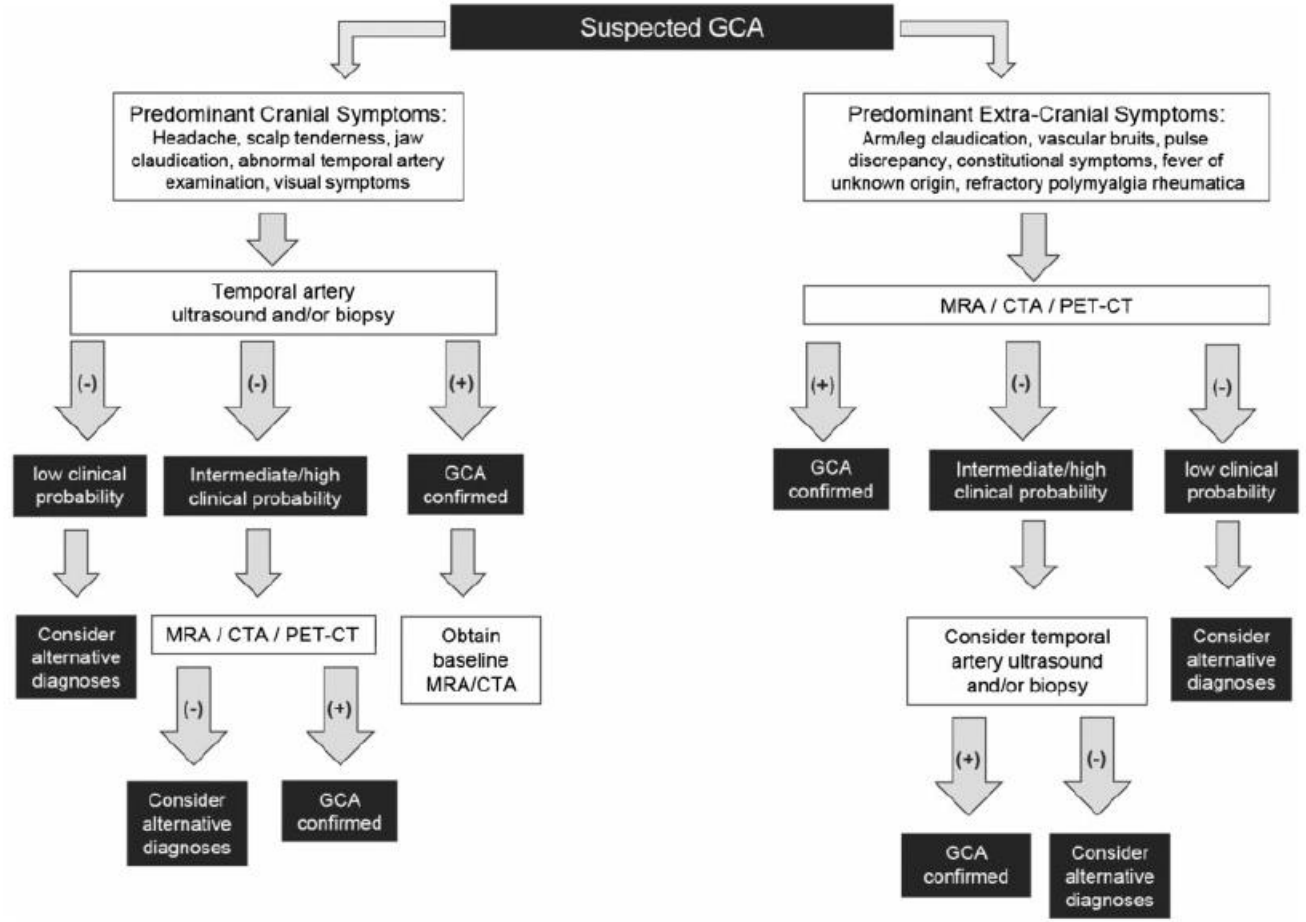
Aorta

Involvement of aorta and its primary branches may be clinically silent

Patient with isolated LV GCA may presents with only constituitional symptoms

Such circumstances requires heightened clinical suspicion and imaging studies to confirm diagnosis

FIG. 1 Proposed algorithm for evaluating patients with suspected GCA



CTA: computed tomography angiography; MRA: magnetic resonance angiography.

Table 2 EULAR recommendations for the use of imaging in LVV in clinical practice

Statement	LoE	LoA
1. In patients with suspected GCA, an early imaging test is recommended to complement the clinical criteria for diagnosing GCA, assuming high expertise and prompt availability of the imaging technique. Imaging should not delay initiation of treatment.	1	9.2 (2.1) 90% ≥8
2. In patients in whom there is a high clinical suspicion of GCA and a positive imaging test, the diagnosis of GCA may be made without an additional test (biopsy or further imaging). In patients with a low clinical probability and a negative imaging result, the diagnosis of GCA can be considered unlikely. In all other situations, additional efforts towards a diagnosis are necessary.	2	9.4 (1.0) 90% ≥8
3. Ultrasound of temporal±axillary arteries is recommended as the first imaging modality in patients with suspected predominantly cranial GCA*. A non-compressible 'halo' sign is the ultrasound finding most suggestive of GCA.	1	9.7 (0.6) 100% ≥8
4. High resolution MRI† of cranial arteries‡ to investigate mural inflammation may be used as an alternative for GCA diagnosis if ultrasound is not available or inconclusive.	2	9.2 (1.1) 90% >8
5. CT† and PET† are not recommended for the assessment of inflammation of cranial arteries.	5	9.5 (1.2) 95% >8
6. Ultrasound, PET, MRI and/or CT may be used for detection of mural inflammation and/or luminal changes in extracranial arteries to support the diagnosis of LV-GCA. Ultrasound is of limited value for assessment of aortitis.	3 (PET and CT) and 5 (MRI and ultrasound)	9.8 (0.6) 100% ≥8
7. In patients with suspected TAK, MRI to investigate mural inflammation and/or luminal changes should be used as the first imaging test to make a diagnosis of TAK, assuming high expertise and prompt availability of the technique.	3	9.1 (1.4) 90% >8
8. PET, CT and/or ultrasound may be used as alternative imaging modalities in patients with suspected TAK. Ultrasound is of limited value for assessment of the thoracic aorta.	3 (CT) and 5 (PET and ultrasound)	9.4 (0.8) 100% ≥8
9. Conventional angiography is not recommended for the diagnosis of GCA or TAK as it has been superseded by the previously mentioned imaging modalities.	5	9.8 (0.6) 100% ≥8
10. In patients with LVV (GCA or TAK) in whom a flare is suspected, imaging might be helpful to confirm or exclude it. Imaging is not routinely recommended for patients in clinical and biochemical remission.	5	9.4 (0.8) 100% ≥8
11. In patients with LVV (GCA or TAK), MRA, CTA and/or ultrasound may be used for long-term monitoring of structural damage, particularly to detect stenosis, occlusion, dilatation and/or aneurysms. The frequency of screening as well as the imaging method applied should be decided on an individual basis.	5	9.3 (1.2) 95% ≥8
12. Imaging examination should be done by a trained specialist using appropriate equipment, operational procedures and settings. The reliability of imaging, which has often been a concern, can be improved by specific training. Suggestions for technical and operational parameters are depicted in box 1.	5	9.8 (0.6) 100% ≥8

Go Slow

- 40–60 mg prednisolone continued until symptoms and laboratory abnormalities resolve (at least 3–4 weeks);
- then dose is reduced by 10 mg every 2 weeks to 20 mg;
- then by 2.5 mg every 2–4 weeks to 10 mg; and
- then by 1 mg every 1–2 months provided there is no relapse.

Guidelines

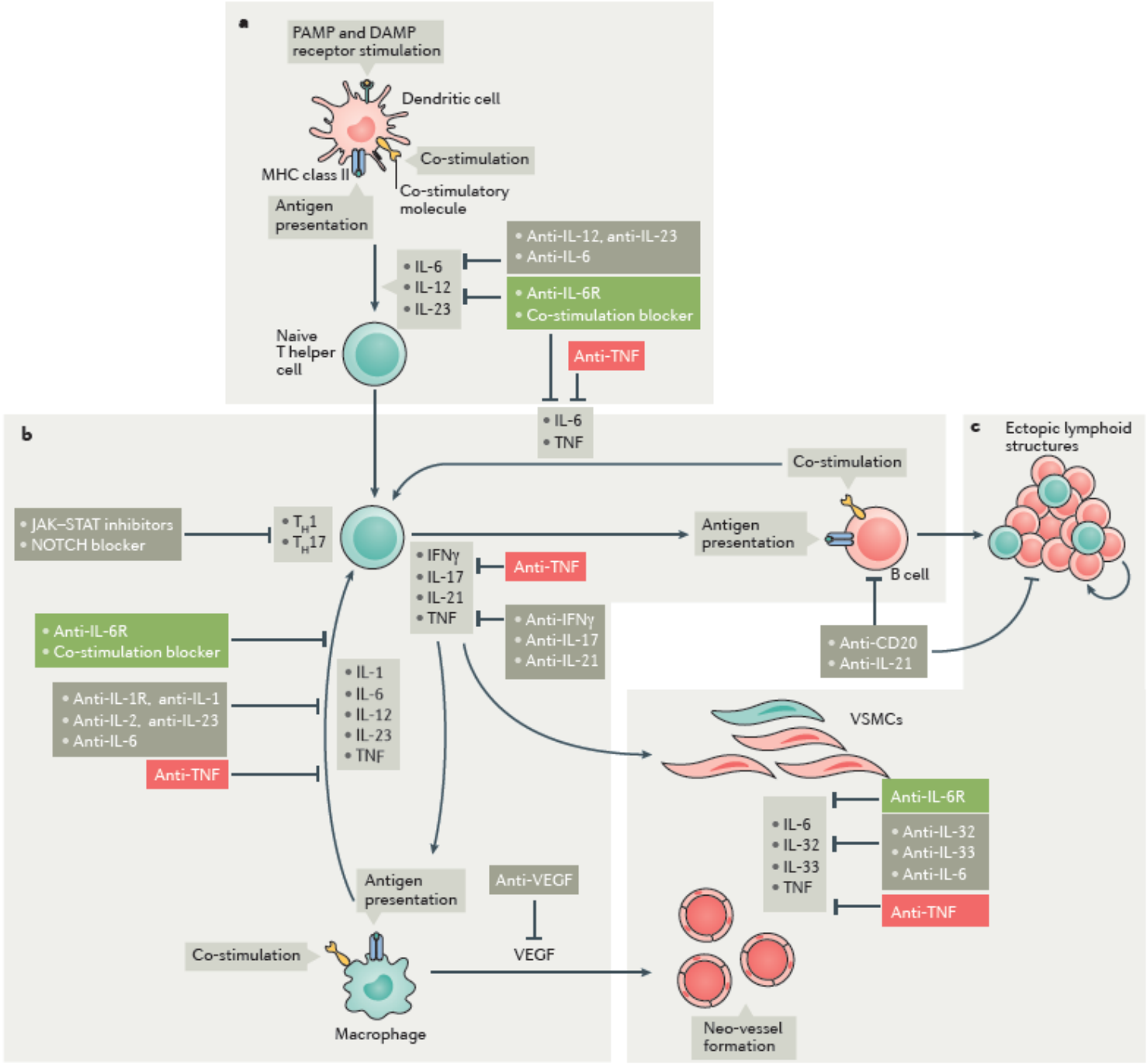
BSR The British Society for Rheumatology

BHPR British Health Professionals in Rheumatology

BSR and BHPR guidelines for the management of giant cell arteritis

BSR guideline Follow up

- At each visit: full blood count, ESR/CRP, urea and electrolytes, glucose.
- Every 2 years: chest radiograph to monitor for aortic aneurysm (echocardiography, PET and MRI may also be appropriate).
- Bone mineral density may be required.


a
PAMP and DAMP receptor stimulation
Dendritic cell
Co-stimulation
MHC class II
Co-stimulatory molecule
Antigen presentation
• IL-6
• IL-12
• IL-23
• Anti-IL-12, anti-IL-23
• Anti-IL-6
• Anti-IL-6R
• Co-stimulation blocker
Anti-TNF
Naive T helper cell
• IL-6
• TNF
b
c
Ectopic lymphoid structures
Co-stimulation
• JAK–STAT inhibitors
• NOTCH blocker
• T_H1
• T_H17
Antigen presentation
B cell
• IFNγ
• IL-17
• IL-21
• TNF
Anti-TNF
• Anti-IFNγ
• Anti-IL-17
• Anti-IL-21
• Anti-CD20
• Anti-IL-21
• Anti-IL-6R
• Co-stimulation blocker
• Anti-IL-1R, anti-IL-1
• Anti-IL-2, anti-IL-23
• Anti-IL-6
Anti-TNF
• IL-1
• IL-6
• IL-12
• IL-23
• TNF
VSMCs
Anti-IL-6R
• IL-6
• IL-32
• IL-33
• TNF
• Anti-IL-32
• Anti-IL-33
• Anti-IL-6
Anti-TNF
Antigen presentation
Anti-VEGF
Co-stimulation
VEGF
Macrophage
Neo-vessel formation

Giant cell arteritis						
Infliximab (TNF blocker)	Randomized, multicentre, double-blinded	44	New GCA (cranial)	54 weeks	Did not achieve primary and main secondary end points	Hoffman 2007 (REF. 134) (full paper)
Etanercept (TNF blocker)	Randomized, multicentre, double-blinded	17	GCA in remission, stable oral prednisone treatment	15 months	Cumulative glucocorticoid dose: 1.5 g in etanercept versus 3.0 g in control group ($p = 0.03$) other outcomes negative	Martinez-Taboada 2008 (REF. 137) (full paper)
Adalimumab (TNF blocker)	Randomized, multicentre, double-blinded	70	New GCA (cranial)	52 weeks	Did not achieve primary and main secondary endpoints	Seror 2014 (REF. 136) (full paper)
Tocilizumab (IL-6 receptor blocker)	Randomized, single-centre, double-blinded	30	New or relapsing GCA	52 weeks	• Complete remission at 12 weeks achieved in 85% of tocilizumab group versus 40% of the control group ($P = 0.03$); complete remission at 52 weeks achieved in 85% of tocilizumab group versus 20% of control group ($P = 0.001$) • Time to relapse: 50 weeks in tocilizumab group versus 25 weeks in control group ($P < 0.001$) • Discontinuation of glucocorticoids: 80% of tocilizumab group versus 20% of control group ($P = 0.004$) • Cumulative glucocorticoid dose: 43 mg/kg in tocilizumab group versus 110 mg/kg in control group ($P < 0.001$)	Villiger 2016 (REF. 18) (full paper)

The GiACTA trial – tocilizumab for giant-cell arteritis

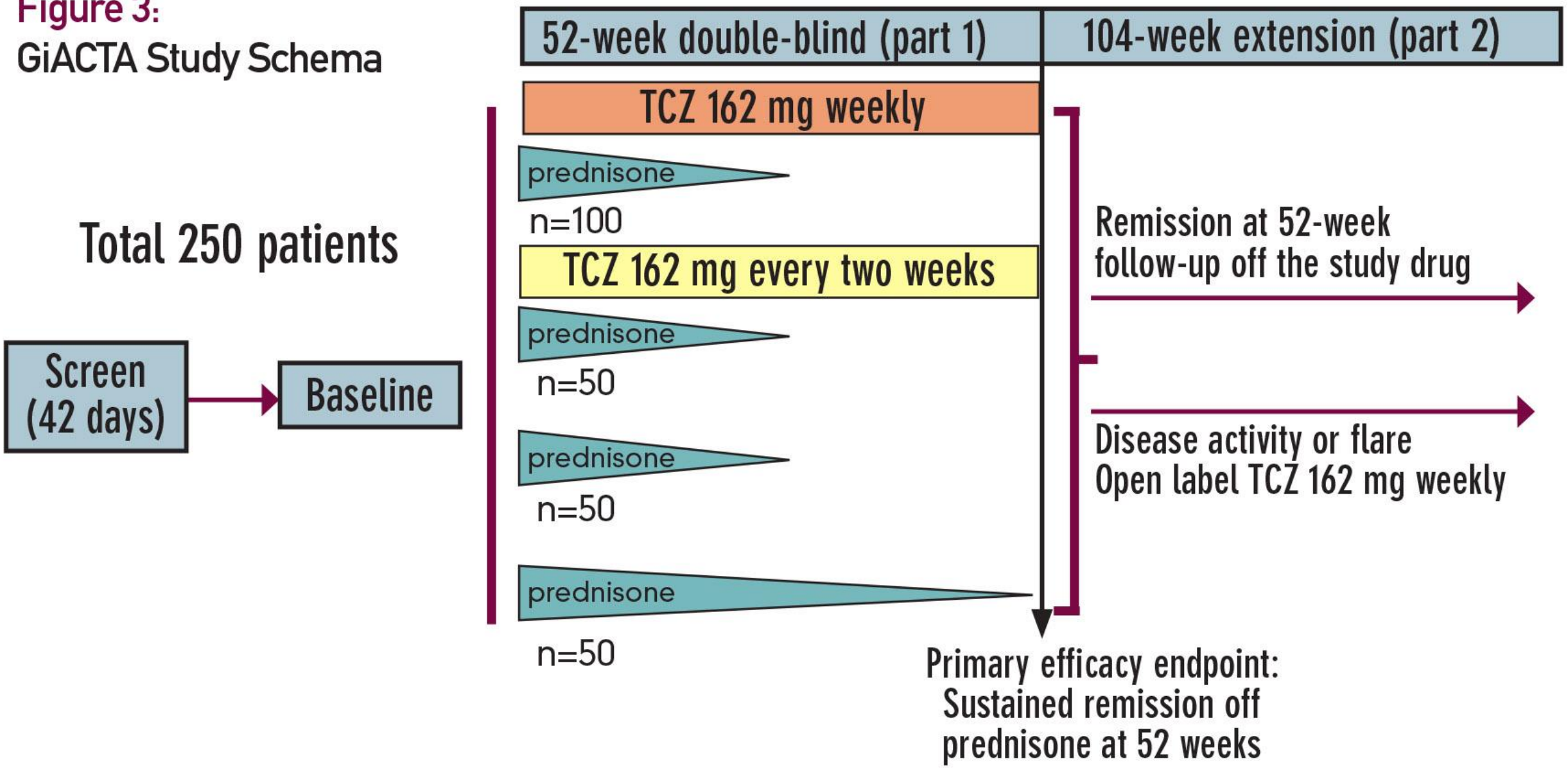
The NEW ENGLAND JOURNAL of MEDICINE

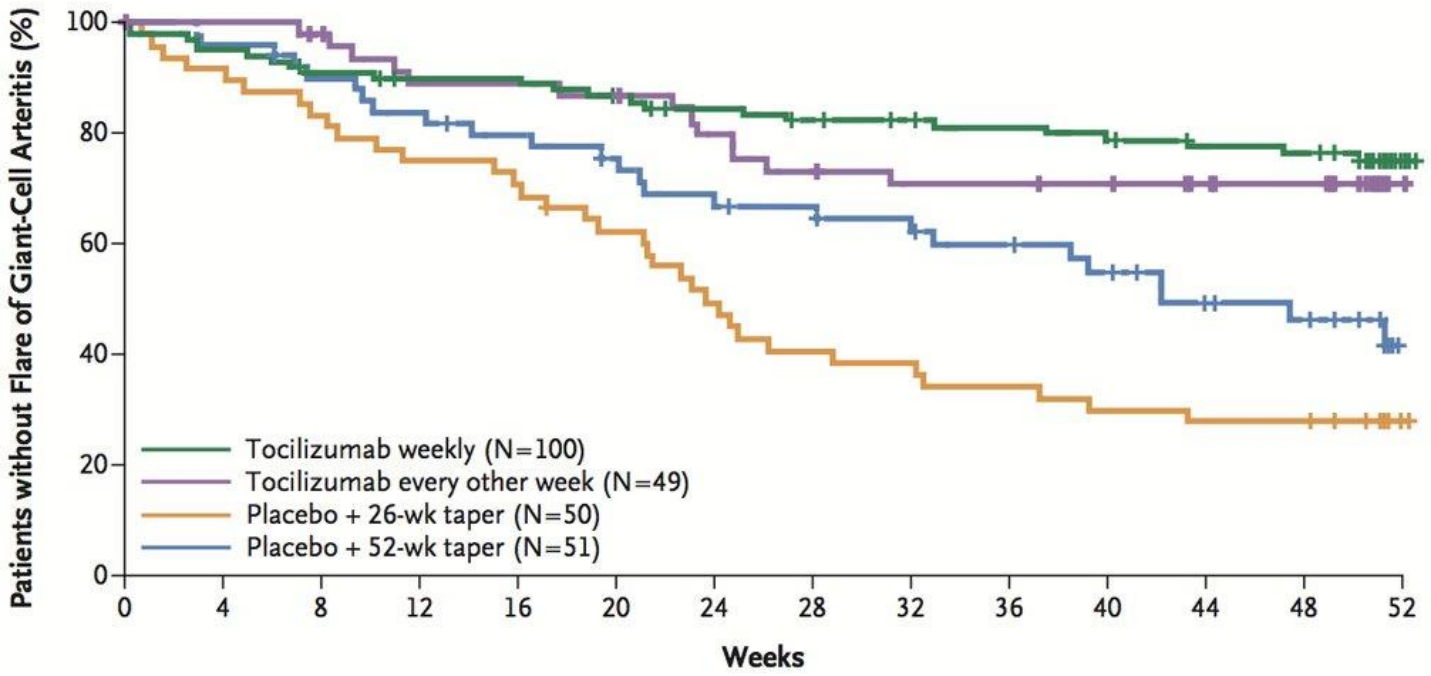
ESTABLISHED IN 1812 JULY 27, 2017 VOL. 377 NO. 4

Trial of Tocilizumab in Giant-Cell Arteritis

J.H. Stone, K. Tuckwell, S. Dimonaco, M. Klearman, M. Aringer, D. Blockmans, E. Brouwer, M.C. Cid, B. Dasgupta, J. Rech, C. Salvarani, G. Schett, H. Schulze-Koops, R. Spiera, S.H. Unizony, and N. Collinson

Figure 3:
GiACTA Study Schema





No. at Risk

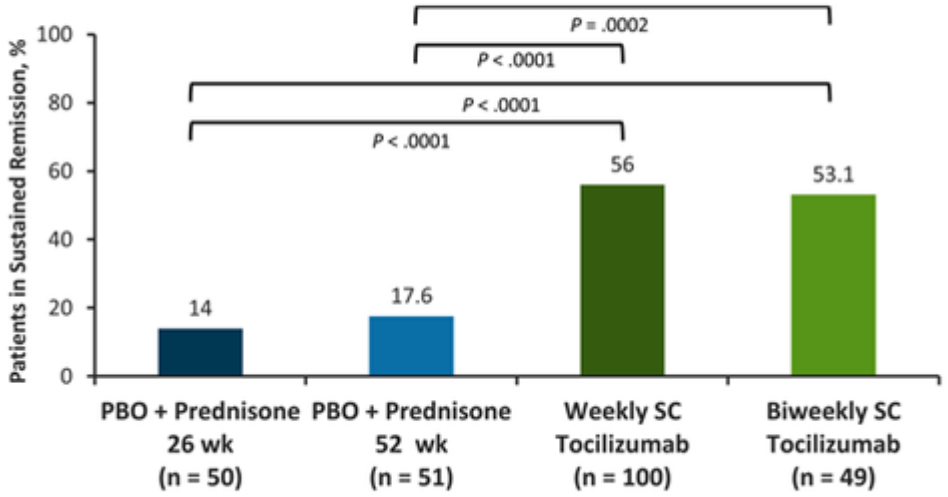
Tocilizumab weekly	100	93	88	85	85	81	77	74	71	69	67	64	63	5
Tocilizumab every other week	49	47	45	40	40	39	35	32	30	30	29	26	24	2
Placebo + 26-wk taper	50	44	40	36	34	29	23	19	18	16	14	13	13	3
Placebo + 52-wk taper	51	48	44	41	38	35	32	30	28	25	22	17	15	0

Figure 2. Time to First Flare after Clinical Remission of Giant-Cell Arteritis in All Patients.

Patients who never had remission were considered to have had a flare at week 0 (data were censored [tick marks] at that time point). Patients who withdrew from the trial before week 52 had their data censored at the time of withdrawal. The values at week 52 represent patients without flare whose week 52 visit was on day 364 of the trial only for the purpose of plotting time points; the analysis captured all the trial days associated with a week 52 visit, and appropriate censoring was applied. In a comparison with the placebo group that underwent the 26-week taper, the hazard ratio in the group that received tocilizumab weekly was 0.23 (99% CI, 0.11 to 0.46) and the hazard ratio in the group that received tocilizumab every other week was 0.28 (99% CI, 0.12 to 0.66; $P<0.001$ for both comparisons). Absolute values for the two tocilizumab groups could not be evaluated because the median was not reached.

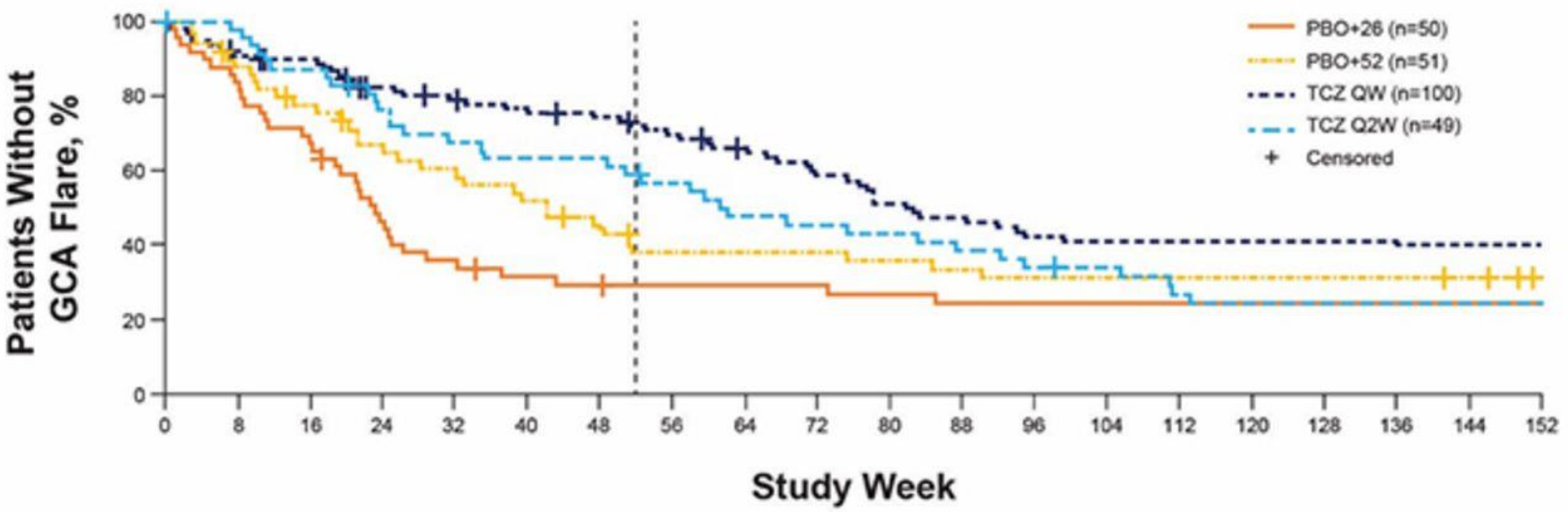
Sustained Remission

Primary and Key Secondary Endpoints



Arthritis and Rheumatology, Stone JH, et al. Copyright © 2016. Reproduced with permission of John Wiley & Sons, Inc.

Figure 1. Kaplan-Meier plot of time to first flare over 3 years (double-blind and part 2 periods; censored for open-label TCZ; ITT population).



No. of Patients

PBO+26	50	45	41	35	33	28	22	18	17	15	14	13	13	12	12	12	12	12	12	11	11	11	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
PBO+52	50	47	43	40	37	34	31	29	28	26	24	21	20	16	16	16	16	16	16	15	15	15	14	13	13	13	13	13	13	13	13	13	13	13	13	13	12	11	9
TCZ QW	100	93	88	85	85	79	75	72	70	68	66	65	64	60	58	55	53	50	47	46	41	38	38	36	34	33	33	33	33	33	33	33	33	33	33	32	32	32	32
TCZ Q2W	49	47	46	41	41	39	35	32	31	29	29	29	29	27	25	23	21	21	20	19	19	18	17	17	15	14	14	13	11	10	10	10	10	10	10	10	10	10	10

Patients never in remission were censored at day 1. Patients who withdrew were censored from the time of withdrawal. Dashed line indicates start of part 2.

John H. Stone et al. Ann Rheum Dis 2019;78:145-146

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Questions