"What's New and What's Coming Down The Pike In GCA Treatment?"

Advances in Rheumatology 2021

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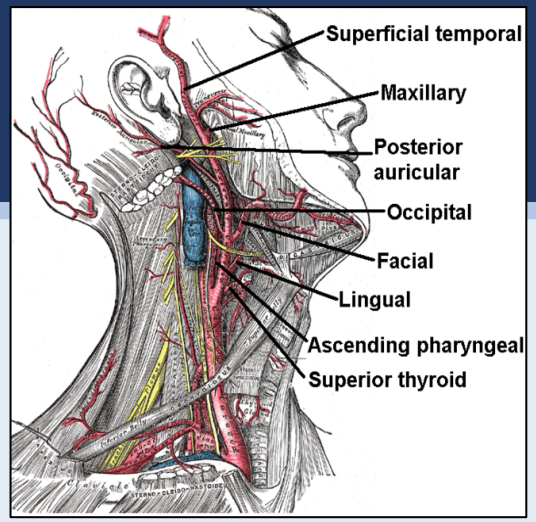
DISCLOSURES

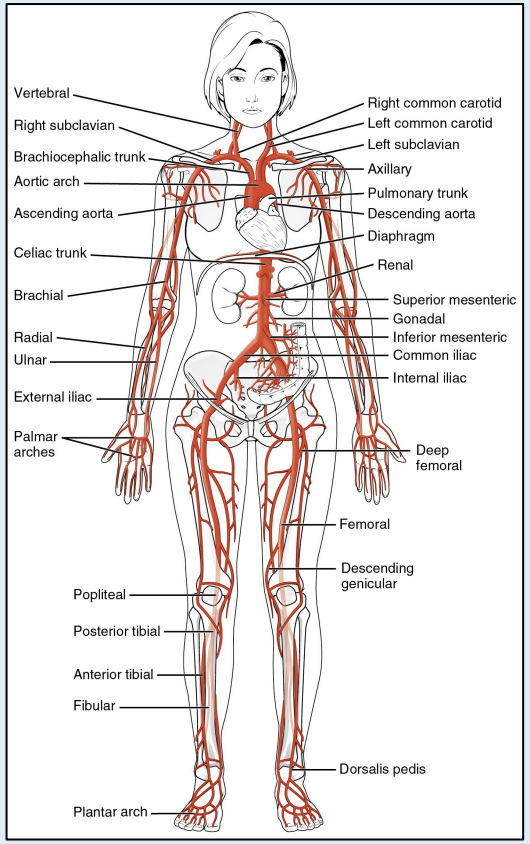
- Roche/Genentech, research support
- Kaniksa, consulting
- Sanofi, consulting
- Janssen, research support and consulting

Most frequent type of vasculitis in adults



Definition

- Large / medium sized-vessel vasculitis
- Granulomatous inflammation
- Aorta and main aortic branches
- Extracranial carotid system and the ophthalmic circulation



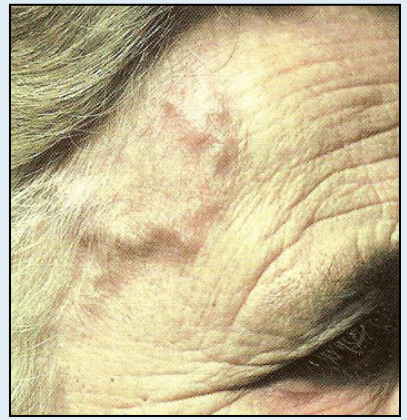
Epidemiology

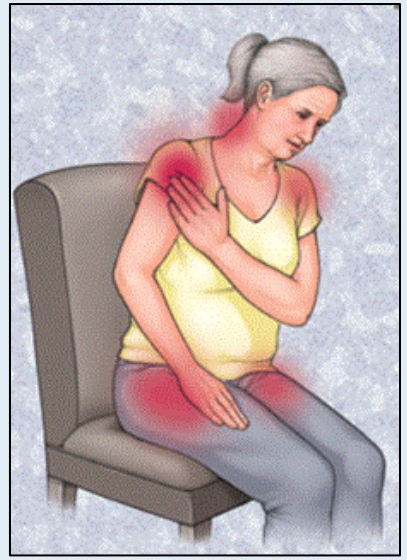
- Most common type of vasculitis in adults
- Elderly (peak age ~72 years)
- Caucasian population
- Lifetime risk 0.5% men - 1% women
- ~220,000 cases in the United States
- Significant morbidity without overall increased mortality

Salvarani at al. Nat Rev Rheumatol 2012

Common clinical manifestations

- Cranial symptoms:
  1) New onset headaches
  2) Scalp tenderness
  3) Jaw claudication
  4) Temporal artery abnormalities
  5) Visual symptoms (blindness 10-20%)





- Polymyalgia rheumatica (PMR) symptoms
- Constitutional symptoms
- Laboratory abnormalities (suggestive, but not specific)
  - Increased inflammatory markers (90-95%)
  - Mild to moderate anemia, thrombocytosis, rarely leucocytosis

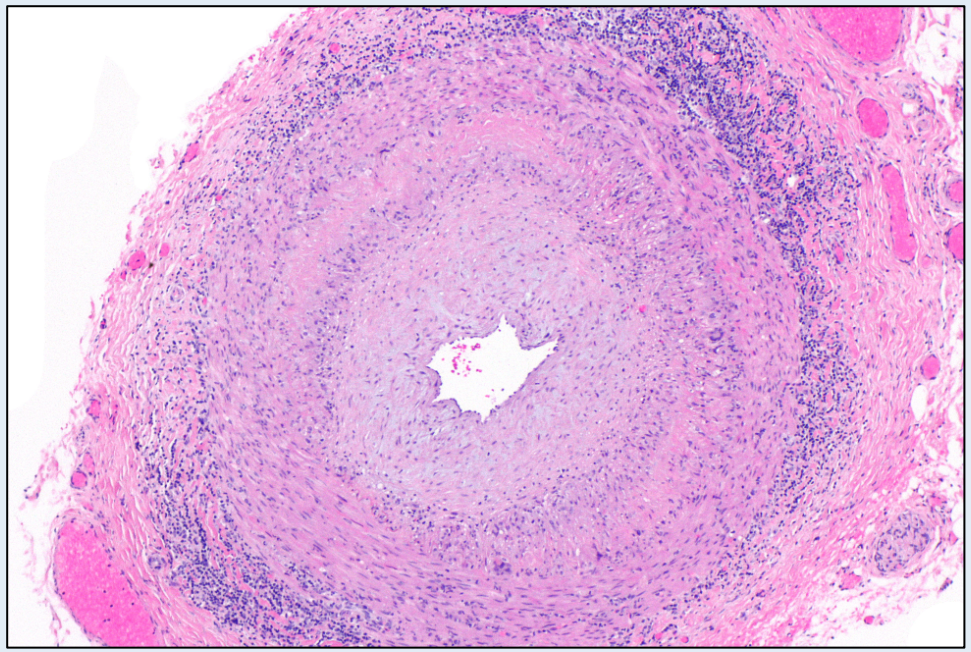
Salvarani at al. Nat Rev Rheumatol 2012

Diagnosis - temporal artery biopsy

2021 American College of Rheumatology / Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis

Conditional recommendations

- Initial diagnostic test
- Unilateral over bilateral biopsies
- Length > 1 cm
- Within 2 weeks of starting glucocorticoids

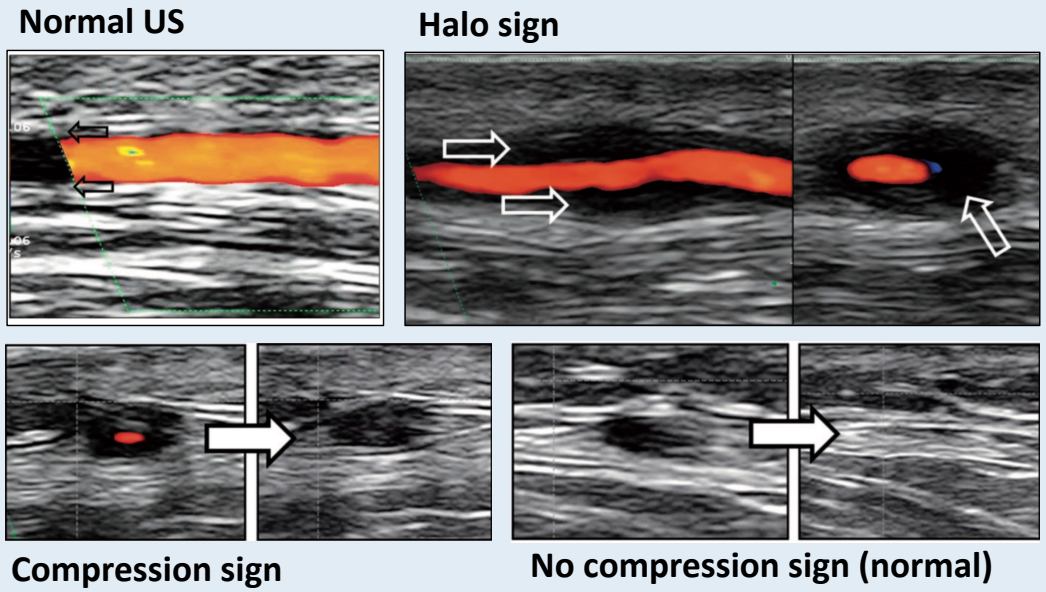


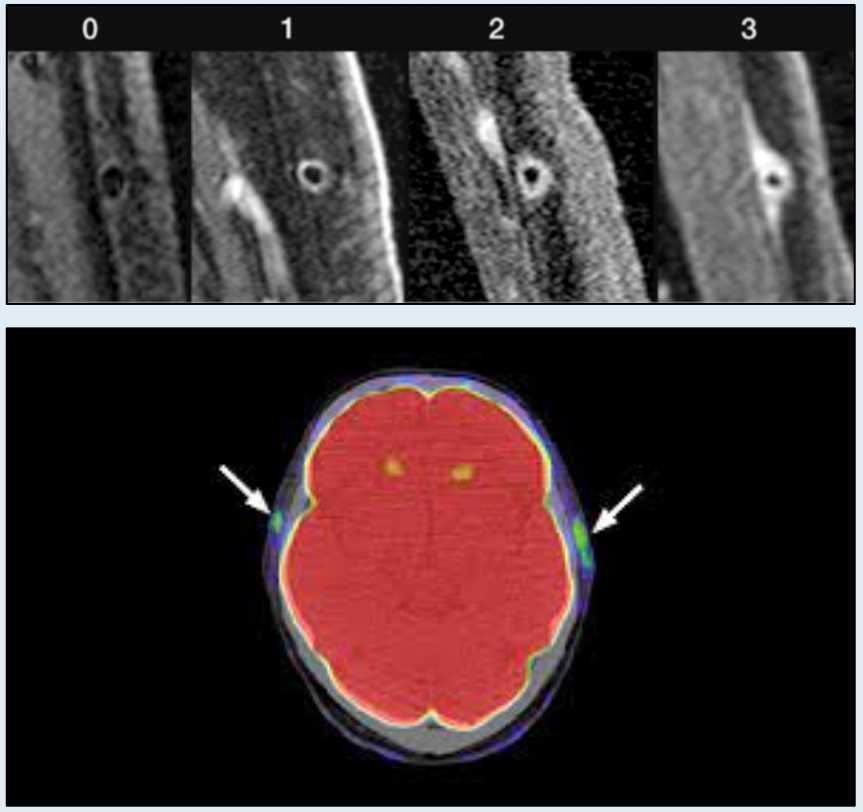
Maz et al. Arthritis Rheum 2021

Diagnosis - vascular imaging

Superficial cranial arteries

- **Vascular ultrasound (US)** - Initial test recommended by the 2018 EULAR LVV imaging guidelines
- Magnetic resonance imaging (MRI)
- PET/CT



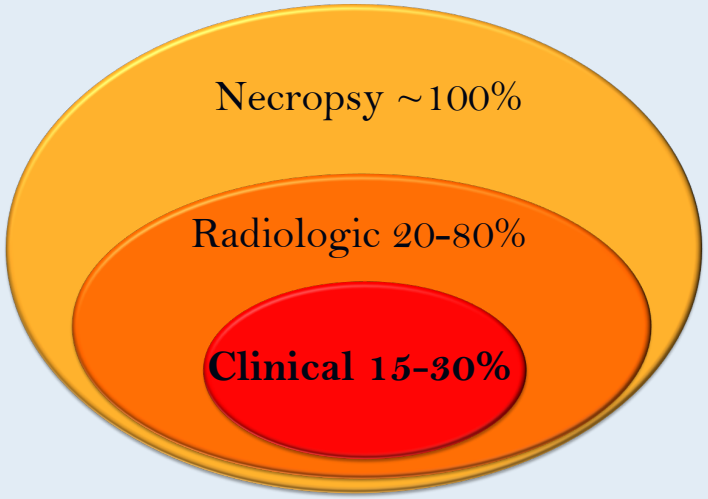


Dejaco et al. Ann Rheum Dis 2018

Diagnosis - vascular imaging

Large arteries

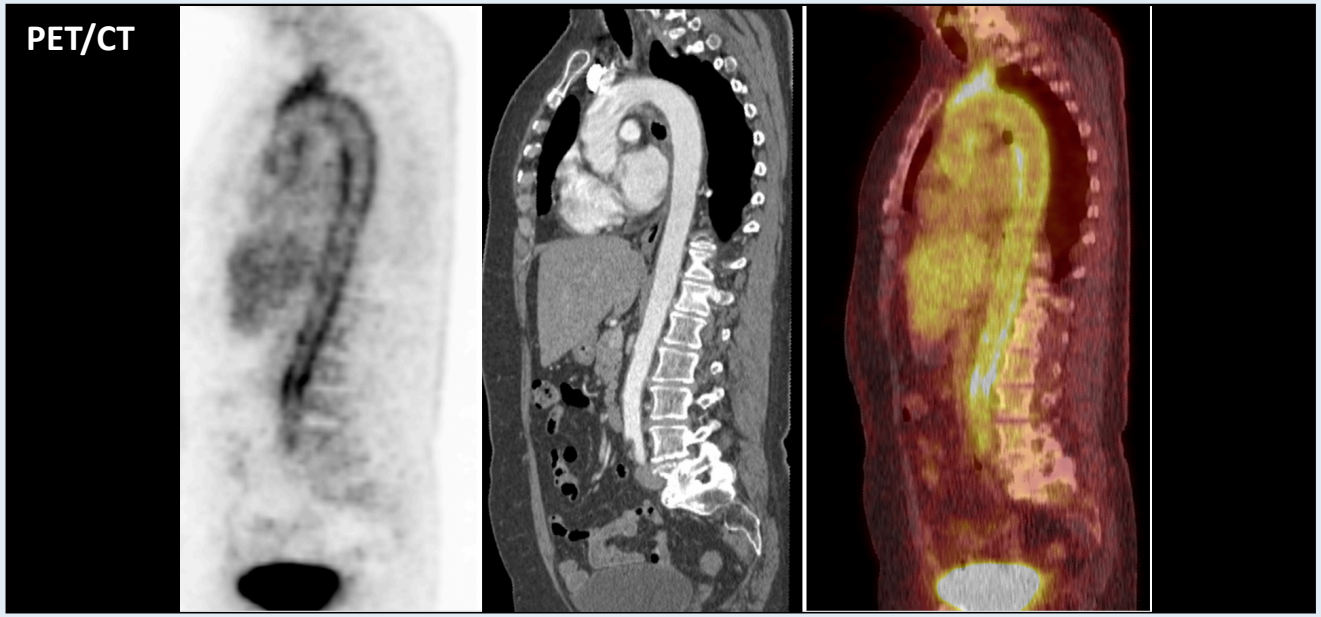
- Computed tomography angiography (CTA)
- MRI / MR angiography (MRA)
- Positron emission tomography (PET)
- PET/CTA and PET/MR
- Vascular ultrasound



Large vessel involvement

Radiologic lesions - "lumens and walls"

- Wall thickening, edema, contrast uptake and/or ^{18}F-FDG uptake
- Diffuse luminal stenosis, occlusion, and/or aneurysmal dilatation



Oseberg G. Acta Med Scan Suppl 1972; Kerman et al. Sem Arthritis Rheum 2018; Gonzalez-Gay et al. Medicine 2004; Nuenninghoff et al. Arthritis Rheum 2003; Garcia-Martinez et al. Arthritis Rheum 2008, Blockmans et al. Arthritis Rheum 2006; Garcia-Martinez et al. Ann Rheum Dis 2013

Pathophysiology and treatment targets

Agents under investigation

- Results available

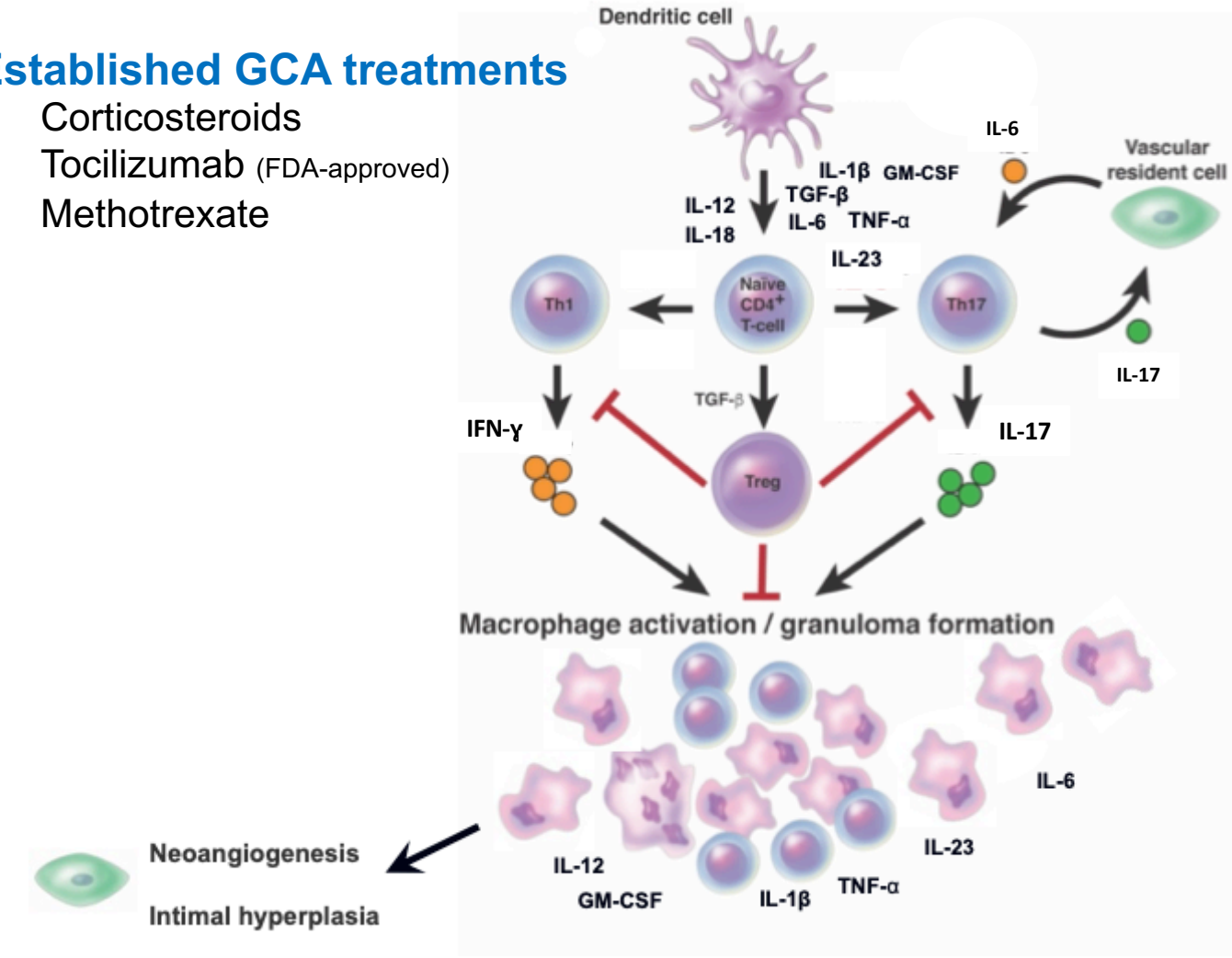
- Mavrilimumab (GM-CSF)
- Abatacept (CD4⁺ T-cell co-stimulation)
- Ustekinumab (IL-12/23 p40)
- Sirukumab (IL-6)

- No results available yet

- Upadacitinib (JAK/STAT)
- Baricitinib (JAK/STAT)
- Guselkumab (IL-23 p19)
- Secukinumab (IL-17)
- Sarilumab (IL-6)
- Abatacept (CD4⁺ T-cell co-stimulation)

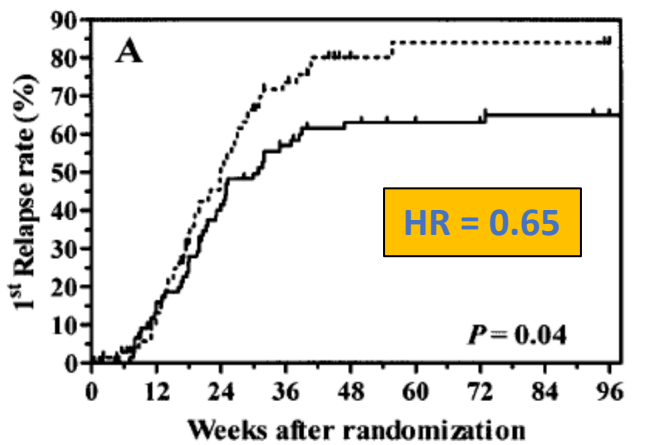
Established GCA treatments

- Corticosteroids
- Tocilizumab (FDA-approved)
- Methotrexate

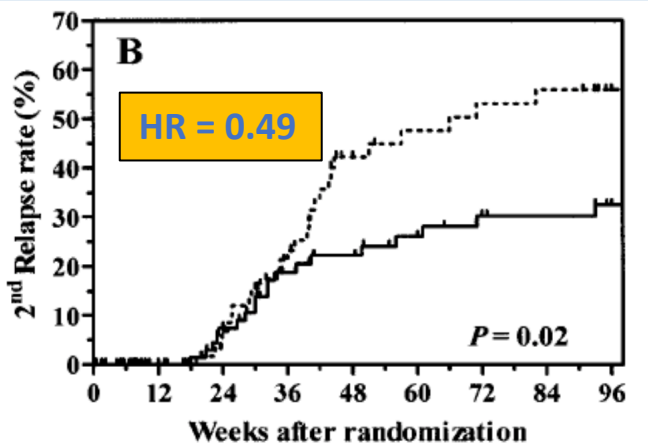


Non-biologic immunosuppressants for GCA

1st relapse



2nd relapse



Mahr et al Arthritis Rheum 2007

Ineffective

- Azathioprine - DaSilva et al. Ann Rheum Dis 1986
- Cyclophosphamide - De Vita at al. Intern Med 1992
- Cyclosporine - Schaufelberger et al. Scand J Rheumatol 2006
- Leflunomide - Adizie et al. Int J Clin Pract 2021

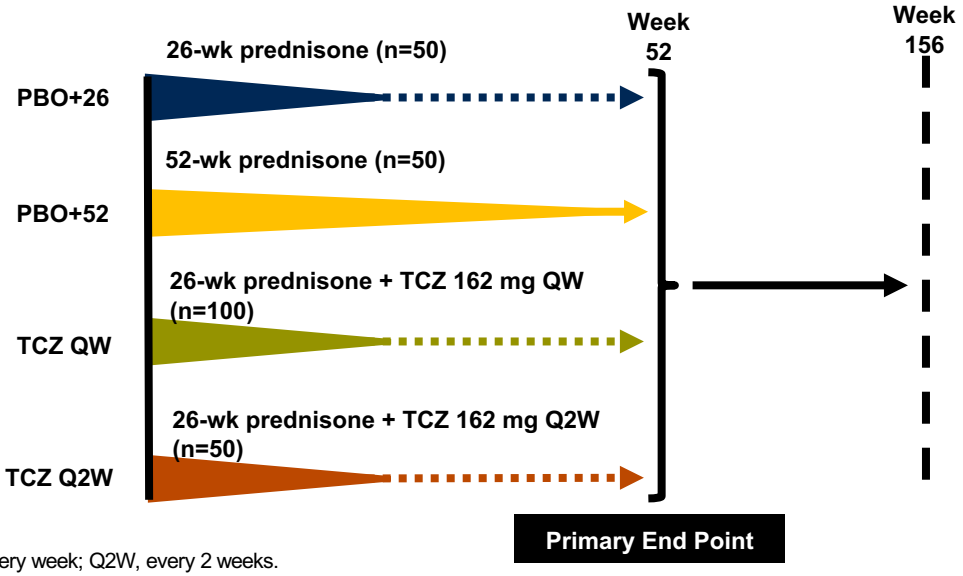
Partially effective

- Methotrexate

Spiera et al. Clini Exp Rheumatol 2001
Hoffman et al. Arthritis Rheum 2002
Jover et al. Medicine 2001

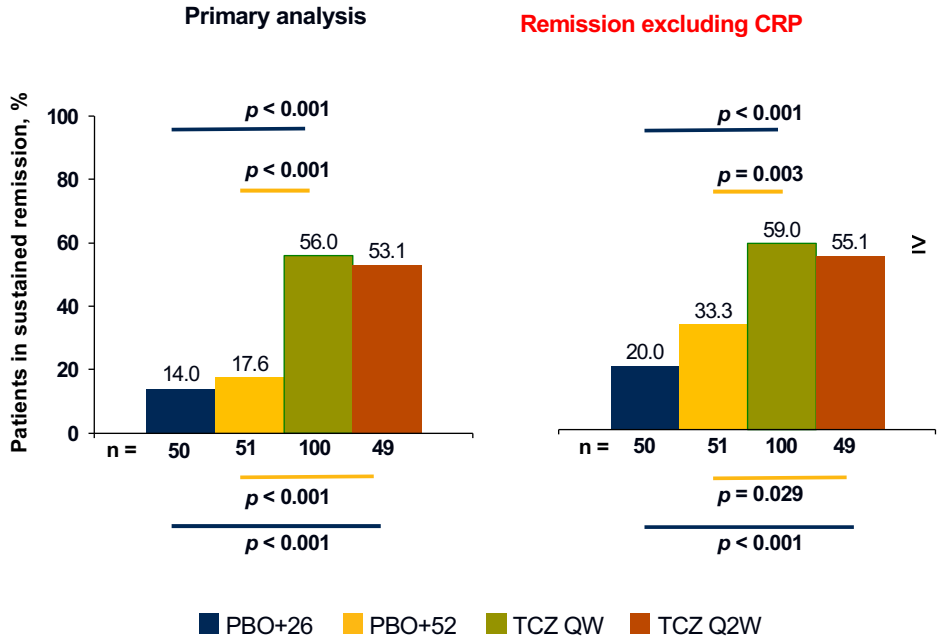
Tocilizumab for GCA (GiACTA study)

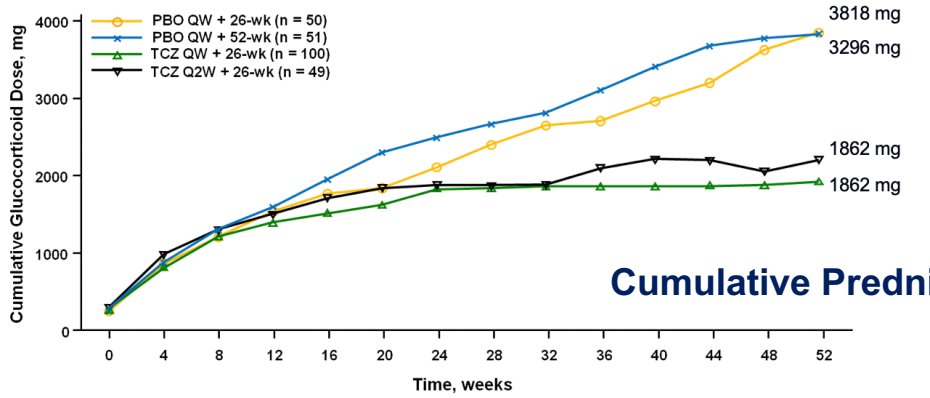
STUDY DESIGN



QW, every week; Q2W, every 2 weeks.

RESULTS - Sustained Remission





Cumulative Prednisone Dose

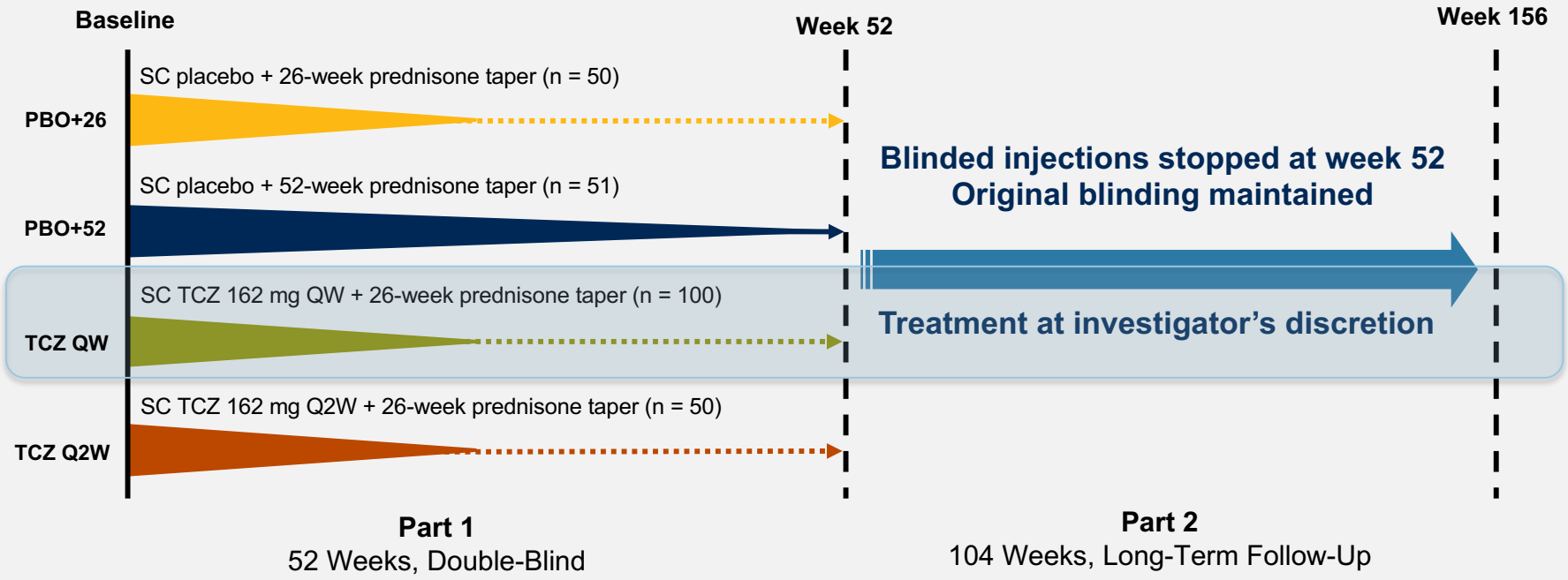
251 patients randomized (2:1:1:1)

Stone et al. N Engl J Med. 2017

Durability of response to tocilizumab

Post hoc analysis of part 2 of the GiACTA trial

Stone et al. Lancet Rheum 2021



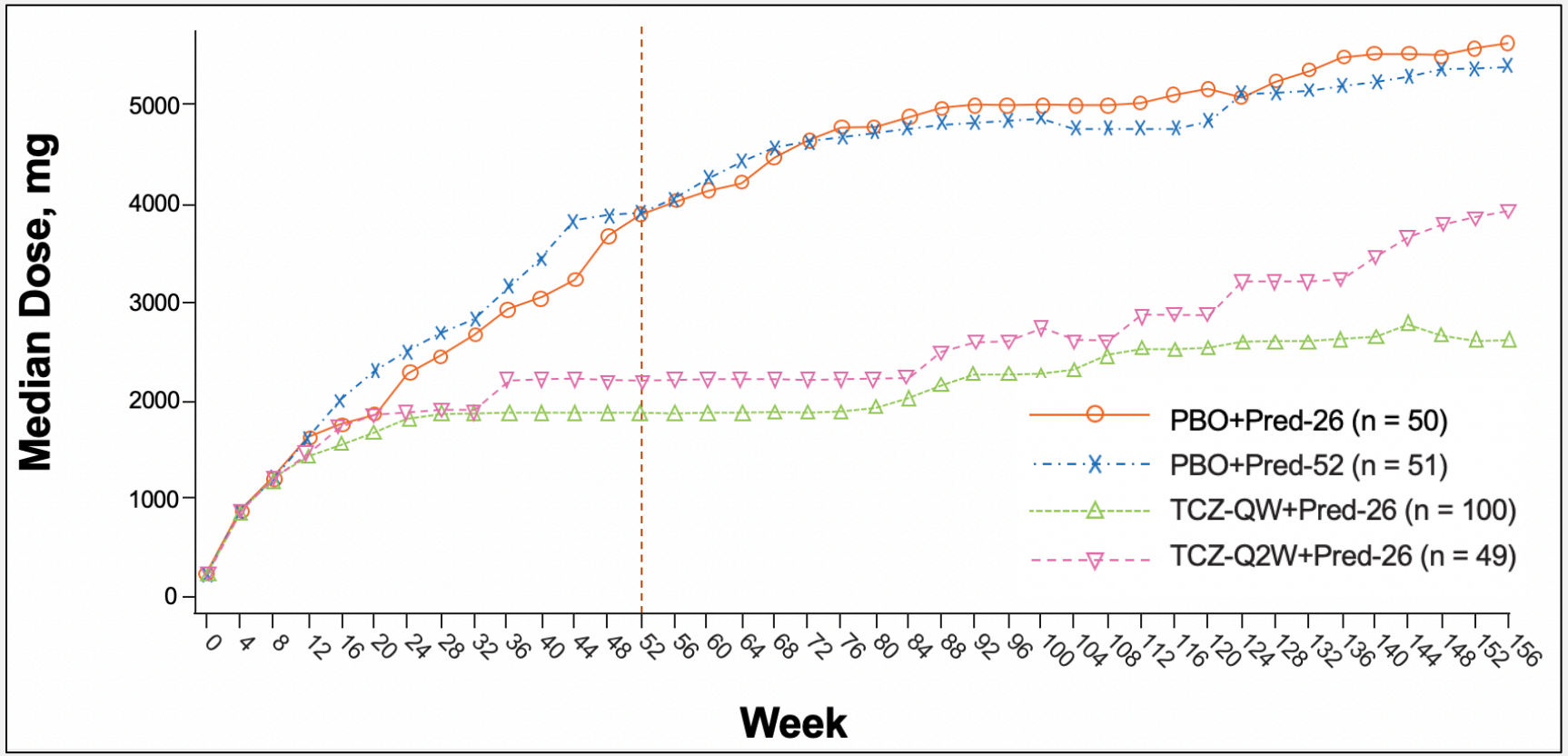
QW, every week; Q2W, every 2 weeks; SC, subcutaneous; TCZ, tocilizumab.

Weekly TCZ arm

85 patients entered Part 2, 81 were in clinical remission, and 59 were off treatment

- 25/59 (42%) maintained the treatment-free clinical remission for 2 years during Part 2

Cumulative prednisone dose over 3 years



5323 mg (3900–6951)

5277 mg (3944–6685)

3948 mg (2352–5186)

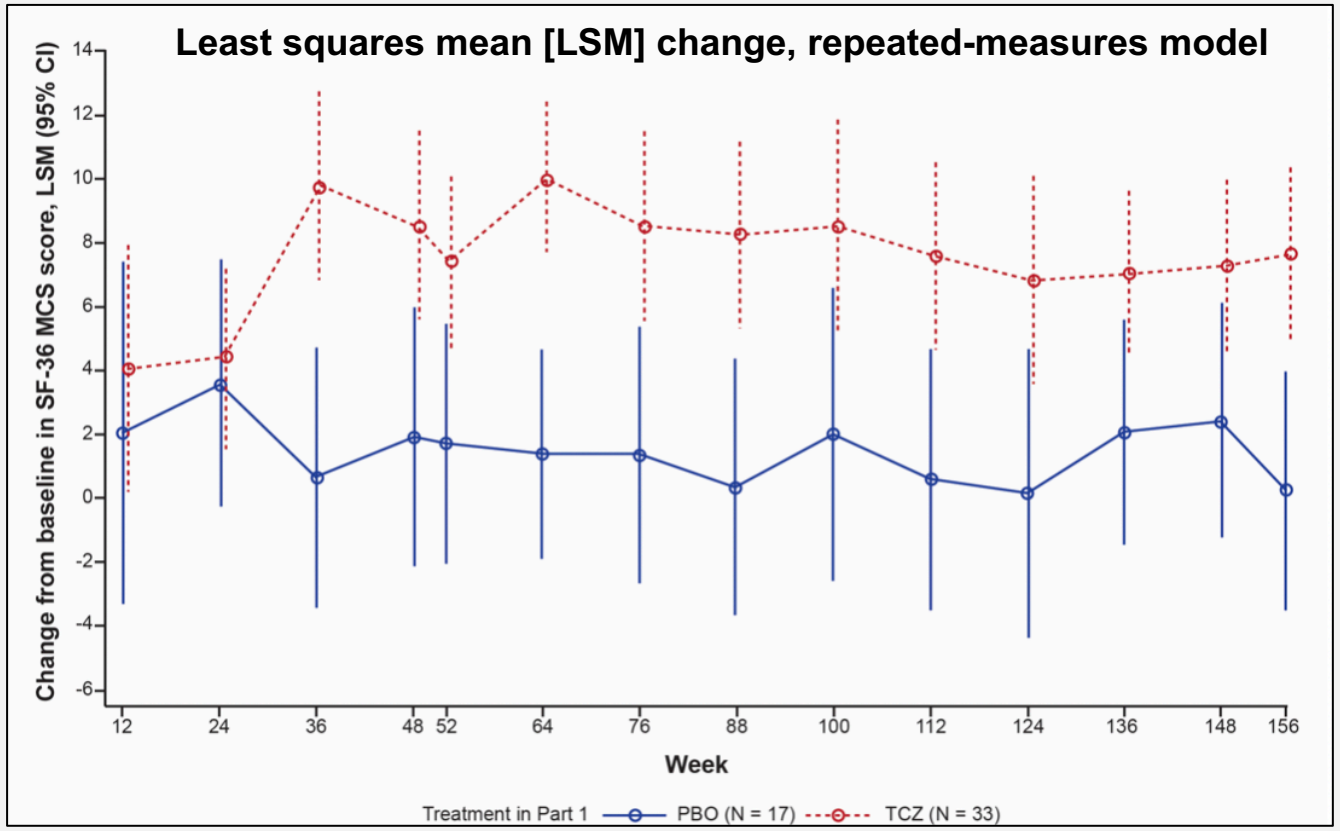
2647 mg (1987–3507)

Stone et al. Lancet Rheum 2021

Health-related quality of life over 3 years

Change from baseline in SF-36 MCS score

Comparison: combined original TCZ (n = 33) and PBO (n = 17) patients achieving clinical remission at week 52 and maintained treatment-free clinical remission in part 2



- SF-36 scores diverged from 36 weeks after baseline
- The difference was statistically significant at week 52 (p = 0.016) and maintained at weeks 100 (p = 0.023) and 156 (p = 0.0019)
- The difference at weeks 52 (5.6), 100 (6.5) and 156 (7.4) exceeded the minimal clinically important difference (MCID) of 2.5.

Stone et al. ACR 2019 (abstract)

Other lessons from GiACTA Part 2

- 46% of GCA patients in sustained remission after successful treatment with 12 months of TCZ (weekly or every other week) had a disease flare within the following 2 years
- Flares occurred after a median of ~24 weeks
- Visual manifestations at the time of flare were rare, and no cases of blindness occurred
- Inflammatory markers were elevated in >75% of the flares (mostly ESR)
- CRP was normal in >50% of the flares
- Re-starting TCZ restored clinical remission

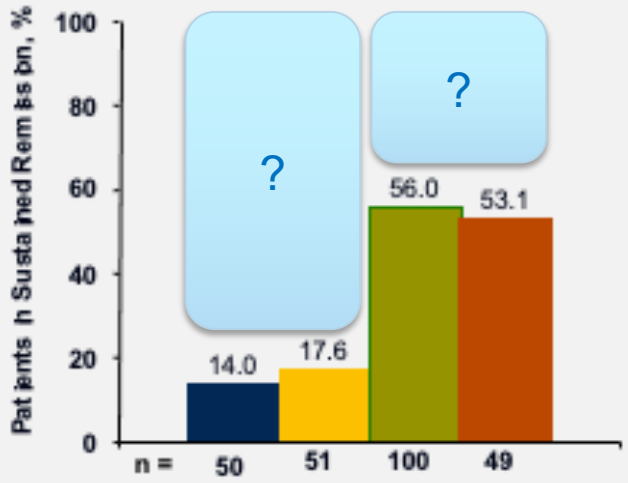
Stone et al. Lancet Rheum 2021, Unizony et al. ACR 2020 (abstract)

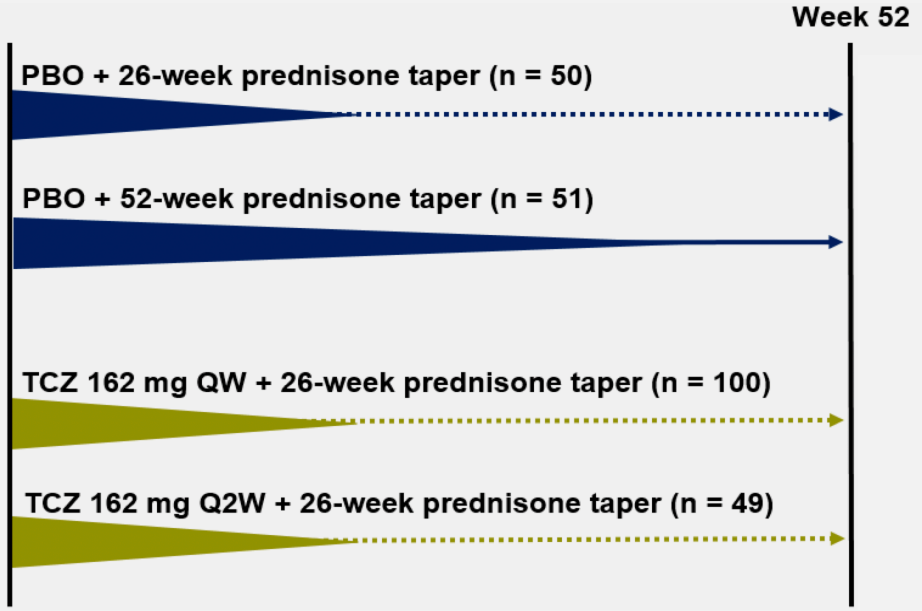
Predictors of treatment failure in GCA

Design

- Secondary analysis of the GiACTA data set

- TCZ plus prednisone arms (**TCZ group**) and PBO plus prednisone arms (**PBO group**) combined





Unizony et al. Ann Rheum Dis 2021

Predictors of treatment failure in GCA

Definitions

- **Treatment response** was defined as the achievement and maintenance of clinical remission from week 12 to week 52 while adhering to the protocol prednisone taper

- **Clinical remission** status was adjudicated by the investigators based on the absence of **disease activity**, defined as GCA signs/symptoms and/or ESR elevation attributable to GCA that required further treatment (e.g., rescue prednisone) regardless of CRP levels

- **Treatment failure** was defined as
  - Inability to achieve clinical remission by week 12 (i.e., **refractory disease**) OR
  - Relapse (i.e., **flare**) between weeks 12 and 52 after clinical remission was achieved by week 12

Unizony et al. Ann Rheum Dis 2021

Predictors of treatment failure in GCA

Predictors

- **Patient-related features** (e.g., demographics)
- **Disease-related features** (e.g., new-onset vs relapsing disease, disease duration, clinical manifestations, and levels of inflammatory markers)
- **Treatment-related features** (e.g., TCZ vs PBO treatment, initial prednisone dose)
- **Health-related quality of life** (HRQoL) patient-reported outcomes (PROs):
  - Patient Global Assessment of Disease Activity (PtGA) score
  - Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score
  - 36-Item Short-Form Survey Instrument (SF-36) score
  - EuroQoL-5 (EQ-5D) score

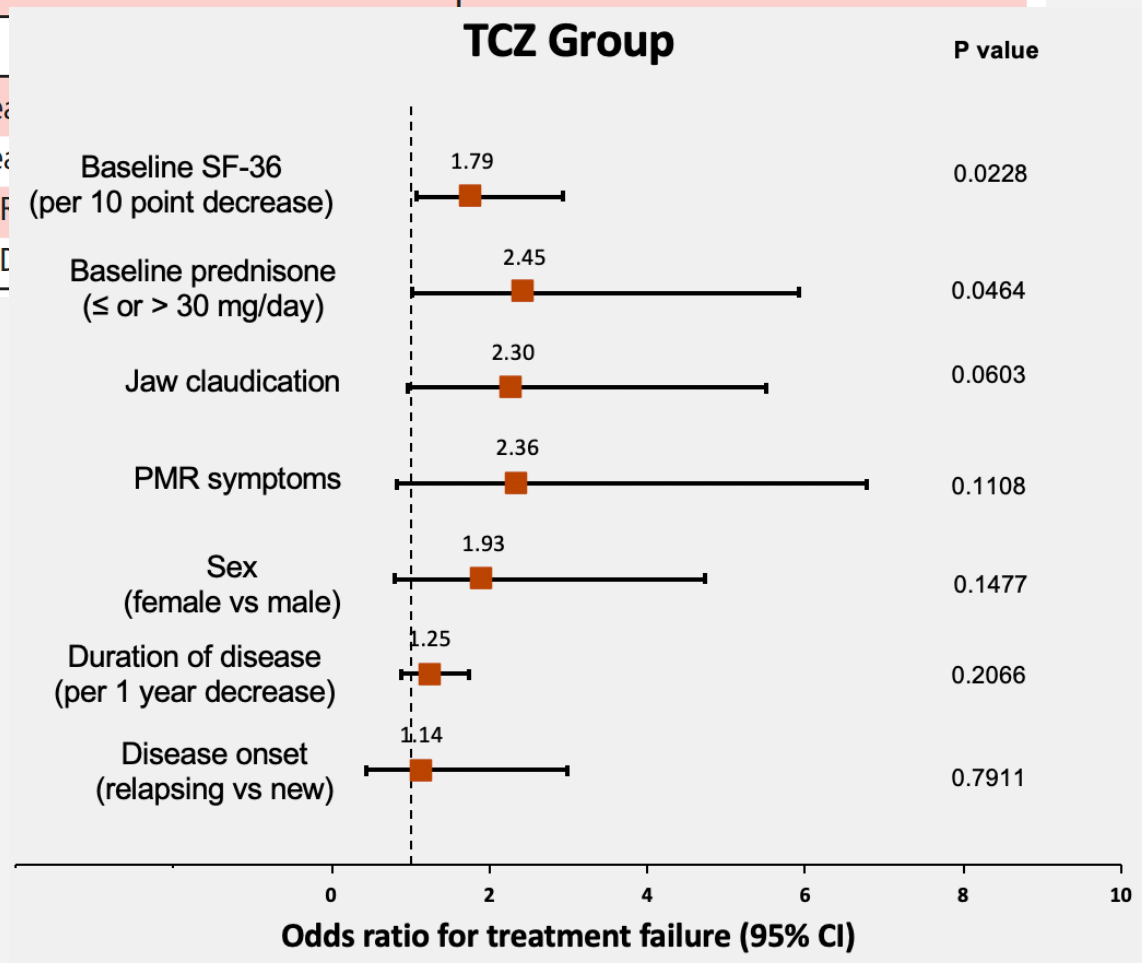
Statistical Methods

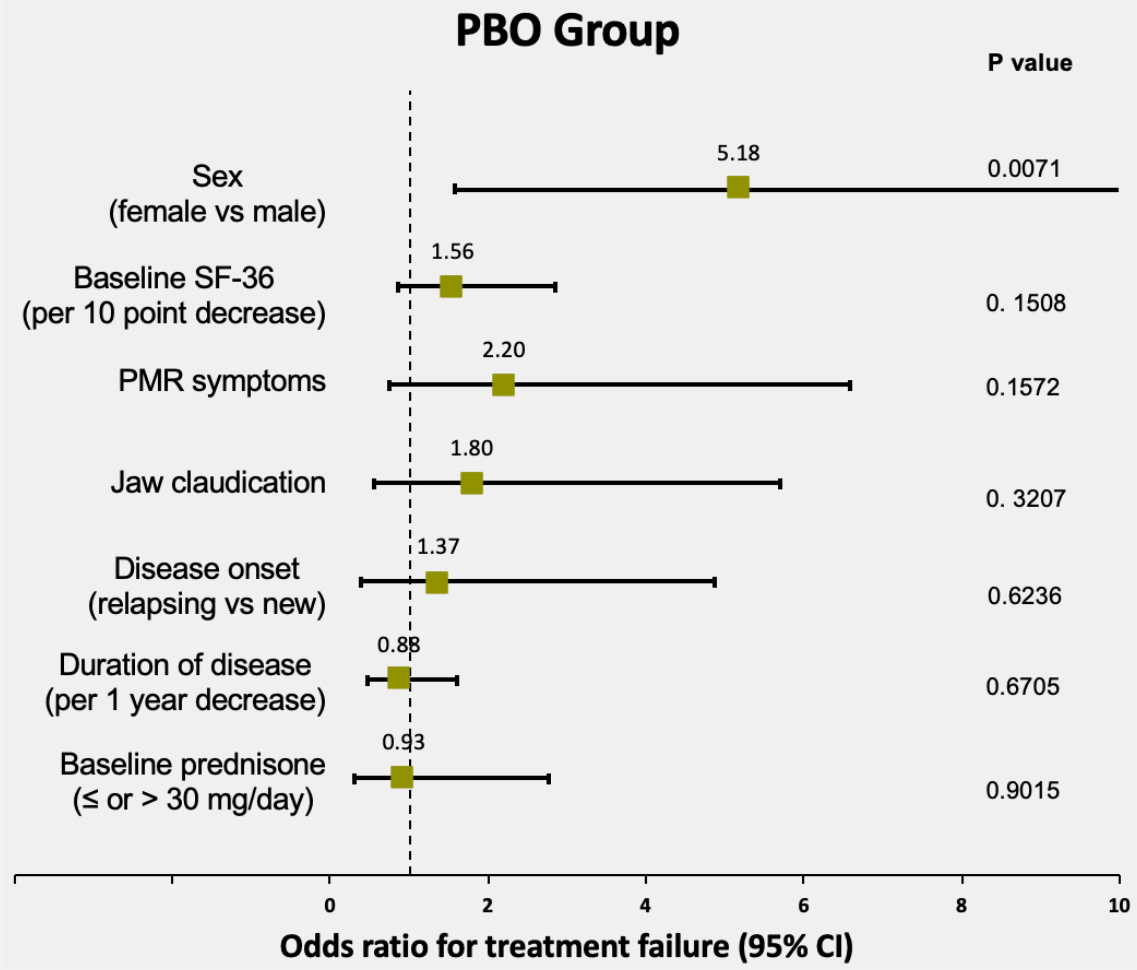
- Continuous and categorical variables were compared using *t* tests and χ^2 tests, respectively
- Logistic regression was applied for multivariate analyses
- Analysis of the entire patient population and according to treatment received (TCZ and PBO)

Unizony et al. Ann Rheum Dis 2021

Predictors of treatment failure in GCA

Table 2 Rates of treatment response and treatment failure





Unizony et al. Ann Rheum Dis 2021

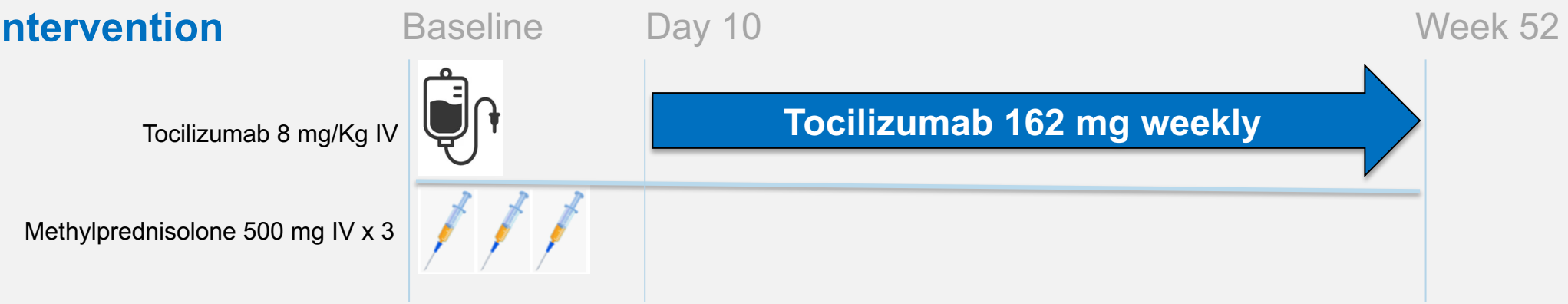
Is less than 6 months of prednisone possible in GCA?

TCZ plus ultra-short steroid course (GUSTO study)

DESIGN

- Prospective, single center, open-label trial of TCZ plus for new onset GCA patients with active disease

Intervention



Endpoints

- Primary endpoint: Remission by day 31 maintained through week 24
- Secondary endpoint: Relapse-free remission at week 52

Results

- 3/12 (25%)
- 13/18 (72%)

ClinicalTrials.gov Identifier: NCT03745586; EULAR 2021 (abstract)

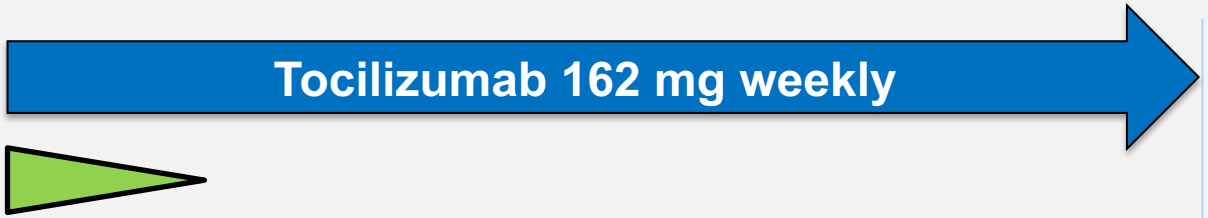
Is less than 6 months of prednisone possible in GCA?

TCZ plus 8 weeks of prednisone for GCA

DESIGN

- Prospective, single center, open-label trial of TCZ plus 8 weeks of prednisone for new onset / relapsing GCA patients with active disease

Intervention



Primary endpoint

- Prednisone-free remission at week 52

ClinicalTrials.gov Identifier: NCT03726749 – PI Unizony

Is less than 6 months of prednisone possible in GCA?

Results (interim analysis, N = 27)

Table 1. Patient Baseline Characteristics

	GCA patients (n = 30)
Age, years: mean (SD)	74 (8.0)
Female sex	18 (60.0)
White race	29 (96.7)
New onset disease	17 (56.7)
Biopsy-proven disease	23 (76.7)
Imaging-proven disease	14 (46.7)
Cranial signs or symptoms	26 (86.7)
PMR symptoms	19 (63.3)
ESR, mm/hour: mean (SD)	50.3 (21.9)
CRP, mg/L: mean (SD)	53.2 (45.8)

Values represent number and (%) unless otherwise specified.
SD, standard deviation; PMR, polymyalgia rheumatica;
ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 2. Outcomes

	GCA patients (n = 27)
Efficacy	
Sustained, prednisone-free remission by week 52	20 (74.1)
Relapse	7 (25.9)
Time to relapse, weeks: mean (SD)	15.1 (13.7)
Clinical manifestations at relapse	
Headaches	3 out of 7 patients
Scalp tenderness	3 out of 7 patients
PMR symptoms	4 out of 7 patients
Jaw claudication	1 out of 7 patients
Safety	
Serious adverse events	4 (3.7)
Cellulitis	1 (3.7)
Cholecystitis	1 (3.7)
COVID-19	1 (3.7)
Fragility fracture	1 (3.7)

Values represent number and (%) unless otherwise specified. SD, standard deviation; PMR, polymyalgia rheumatica

ClinicalTrials.gov Identifier: NCT03726749 – PI Unizony

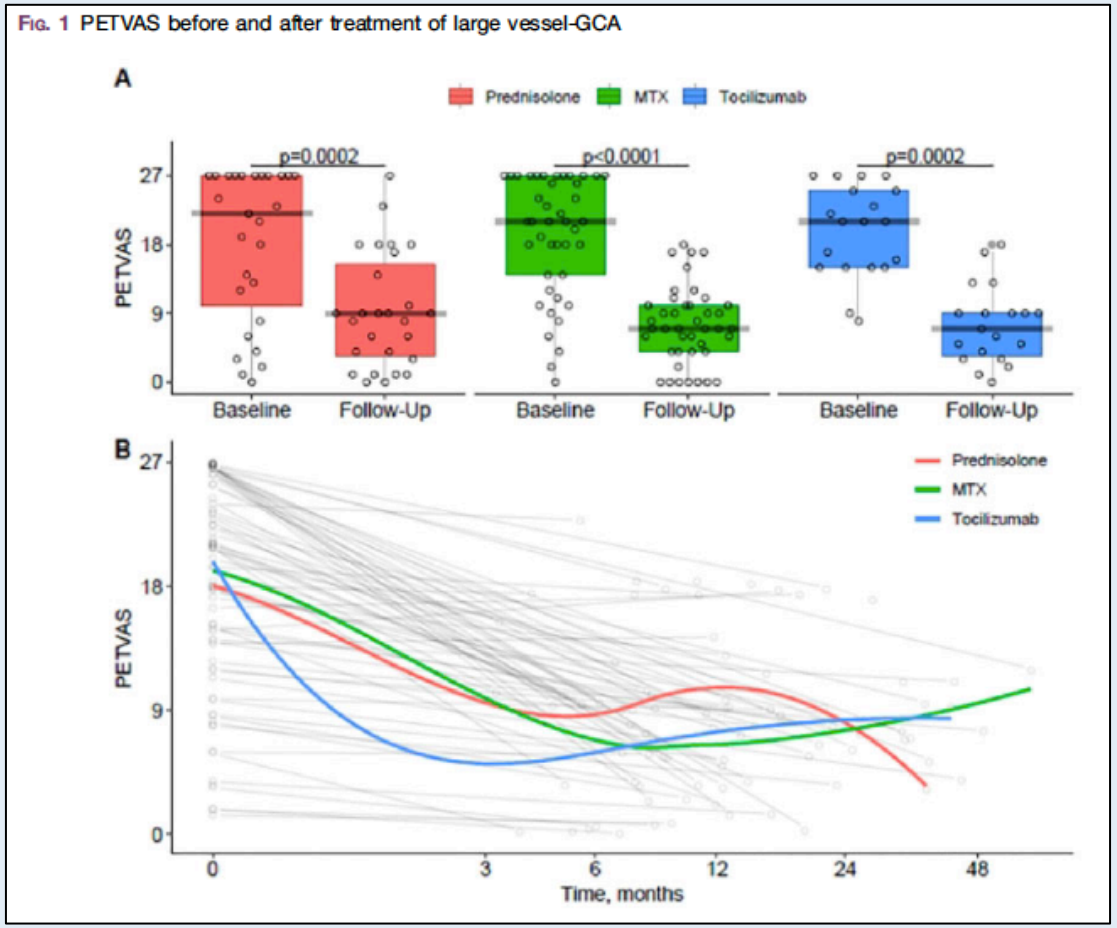
Large vessel involvement response to treatment

RIGA Study (observational)

- Glucocorticoids only (n = 27); MTX (n = 42), TCZ (n = 19)
- PET/CT baseline and ~12 months
- Endpoint: change in PETVAS score (0-27)

RESULTS

Treatment	PETVAS reduction points	Cumulative GC dose (mg)	GC discontinuation
GC alone	- 8.7	5637	4%
MTX	- 11.7	4478	35%
TCZ	- 12.3	2984	80%



Schonau et al. Rheumatology 2021

What's Coming Down The Pike In GCA Treatment?

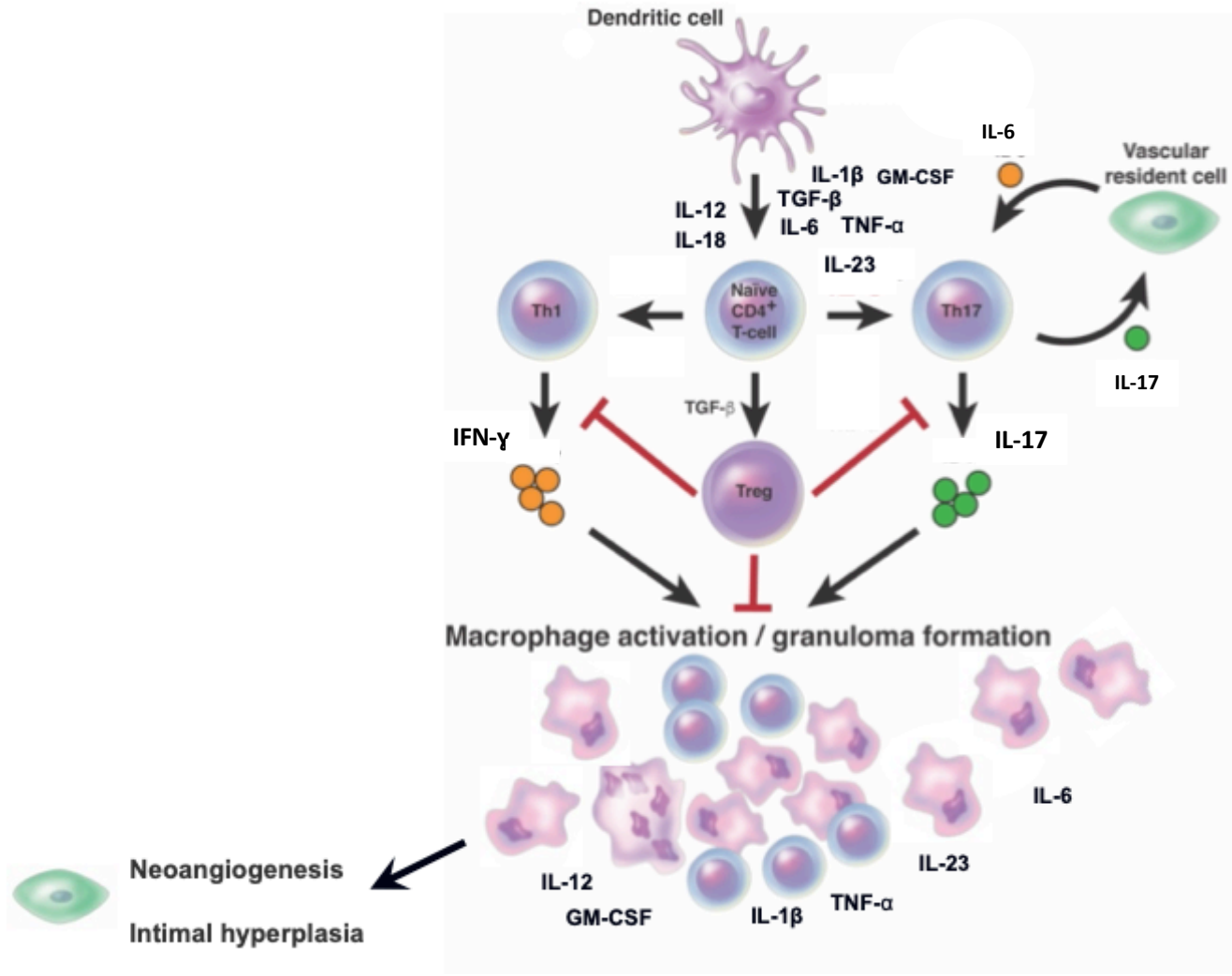
Agents under investigation

Results available

- **Mavrilimumab** - Phase 2 RCT
- **Abatacept** - Phase 2 RCT
- **Ustekinumab** - Uncontrolled
- Sirukumab - RCT terminated

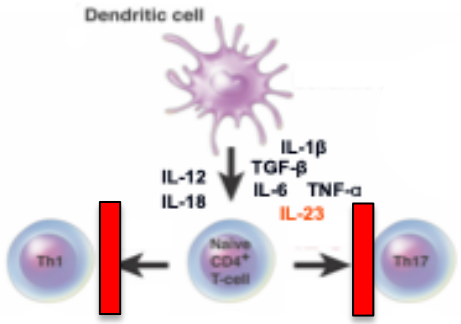
No results available yet

- Upadacitinib - Phase 3 RCT
- Baricitinib - Uncontrolled, complete
- Guselkumab - Phase 2 RCT
- Secukinumab - Phase 2 RCT, complete
- Secukinumab - Phase 3 RCT
- Sarilumab - RCT terminated
- Abatacept



Ustekinumab for GCA

Pathophysiologic rationale for IL-12/23 blockade



DESIGN

- Uncontrolled prospective study
- Relapsing / refractory patients with active (N = 13) or inactive disease (N = 12)
- Ustekinumab (UST) for at least 12 months (90 mg SQ at week 0 and 4, then every 12 weeks)

Endpoints

- Median prednisolone dose before and after UST
- Disease flare

RESULTS

- Mean prednisolone dose from 15 mg to 5 mg
- No relapses reported on UST
- Prednisolone stopped in 6 patients (24%)
- Cumulative prednisolone dose 2.7 grs

Baseline characteristics of 25 GCA patients treated with ustekinumab

Age, years, mean (SD)	70 (7.3)
Female, *n* (%)	20/25 (80)
ACR criteria, *n* (%)	21/25 (84)
Biopsy positive, *n* (%)	19/25 (76)
Temporal artery ultrasound positive, *n* (%)	6/18 (33)
CT angiogram positive, *n* (%)	10/13 (77)
Cranial-ischaemic complications, *n* (%)	5/25 (20)
Vasculitis Damage Index, median (IQR)	1 (0, 2)
Charlson Co-morbidity Index	1 (1, 2)
Disease duration, months, median (IQR)	29 (11.5, 36.5)
Relapses, median (IQR)	2 (1, 3)
Clinical presentation at last relapse	
Cranial, *n* (%)	10 (40)
Polymyalgia rheumatica, *n* (%)	8 (32)
Constitutional, *n* (%)	9 (36)
Large vessel vasculitis, *n* (%)	9 (36)

Conway et al. Seminar Arthritis Rheum 2018

Ustekinumab for GCA

MGH study

DESIGN

- Prospective, single center, open-label trial of UST for new onset / relapsing GCA patients with active disease

Intervention

1) Subcutaneous UST 90 mg

2) Pre-specified 6-month prednisone taper starting at 60 mg, 40 mg, or 20 mg

Primary endpoint

- Prednisone-free remission at week 52

✓ Absence of disease relapse from induction of remission up to week 52
✓ Normalization of ESR (<40 mm/hour) and CRP (<10 mg/L)
✓ Adherence to the protocol prednisone taper

Matza et al. Arthritis Care Res 2020

Ustekinumab for GCA

RESULTS

- Baseline characteristics (N = 13)

	GCA patients (n = 13)
Age, years: mean (SD)	71 (7)
Female sex (%)	11 (85)
White race (%)	13 (100)
New onset disease (%)	5 (39)
Biopsy-proven disease (%)	11 (85)
Imaging-proven disease (%)	4 (31)
Cranial signs or symptoms (%)	13 (100)
PMR symptoms (%)	8 (62)
ESR, mm/hour: mean (SD)	41 (16)
CRP, mg/L: mean (SD)	50 (39)

- Target enrollment of 20 patients
- Enrollment closed prematurely after 7 of the initial 10 patients relapsed
- A total of 13 patients were enrolled between February 2017 and July 2018

Matza et al. Arthritis Care Res 2020

Ustekinumab for GCA

RESULTS

- Efficacy

	GCA patients (n = 13)
Prednisone-free remission by week 52 (%)	3 (23)
Alternative definition of prednisone-free remission by week 52 (%)	6 (46)
Disease flare (%)	7 (54)
Clinical features at disease relapse* (%)	
Cranial signs or symptoms (%)	3 (43)
PMR symptoms (%)	7 (100)
ESR, mm/hour: mean (SD)	49 (26)
CRP, mg/L: mean (SD)	40 (34)
Time to flare, weeks: mean (SD)	23 (7)
Number of UST doses received, mean (SD)	4 (1)
Prednisone dose, mg/day: mean (SD)	3 (3)

*Analyses limited to the 7 patients that relapsed.

Conclusion: UST in combination with a 6-month prednisone taper was not associated with a clinically significant rate of sustained, prednisone-free remission in this cohort of GCA patients

Matza et al. Arthritis Care Res 2020

Ustekinumab for GCA

Conway et al.

- UST 90 mg SQ at week 0, week 4, and Q3 months
- **Prednisolone discontinuation not required**
- 75% of patients were still on prednisone (median dose 5 mg/day) by week 52

Matza et al.

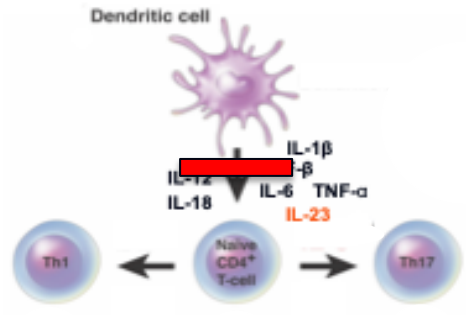
- UST 90 mg SQ at week 0, week 4, and Q2 months
- **Prednisone taper over 6 months per protocol**

Conway et al. Semin Arthritis Rheum 2018, Matza et al. Arthritis Care Res (Hoboken). 2020

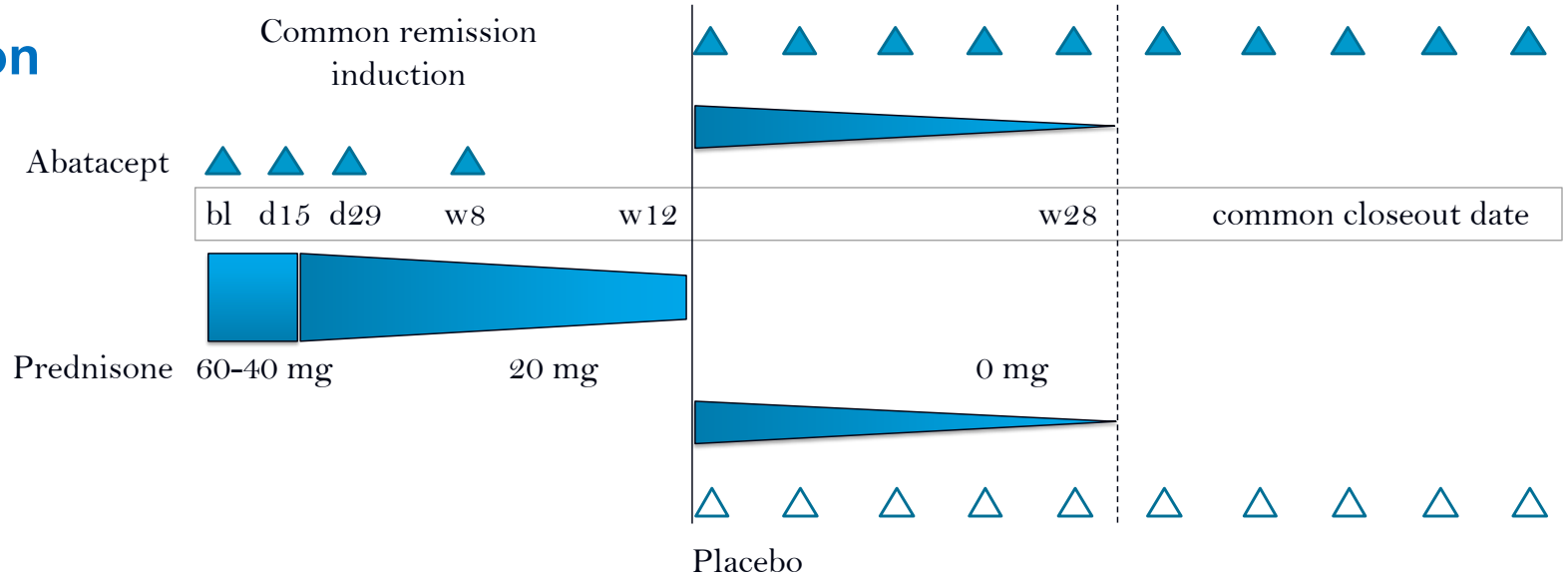
Abatacept for GCA

DESIGN

- Phase II, randomized, double-blind, placebo-controlled trial – withdrawal randomization



Intervention



Primary endpoint

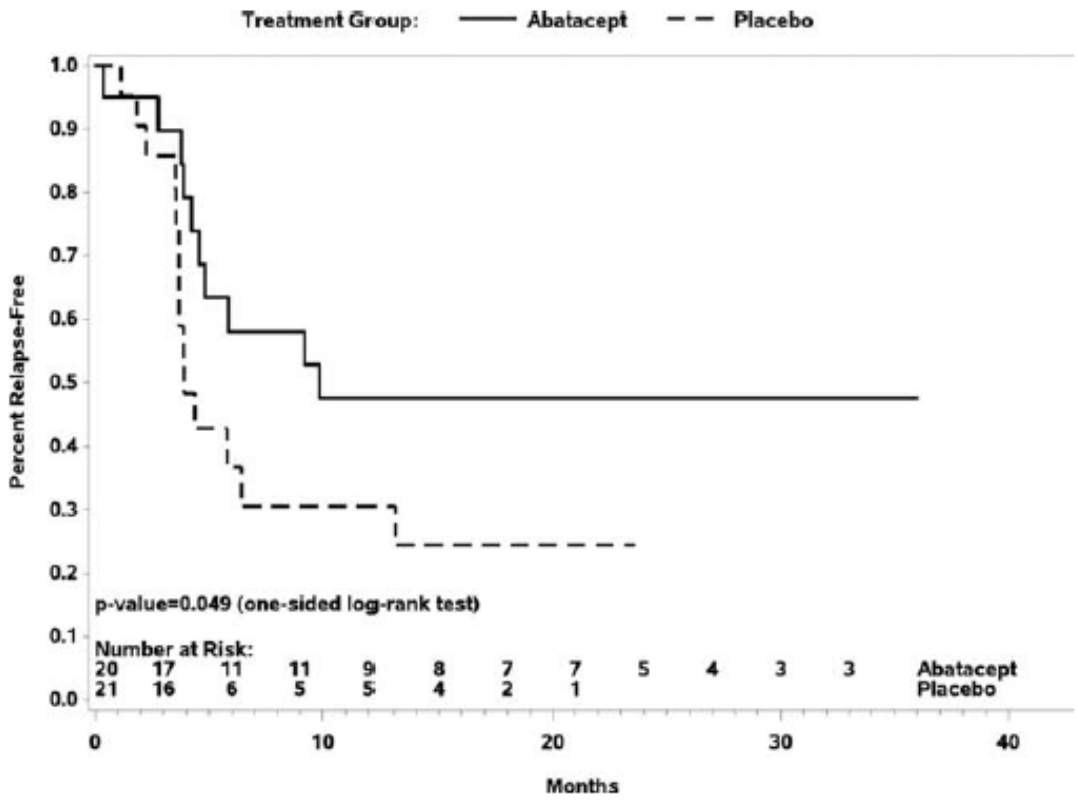
- Relapse-free survival (duration of remission)

Langford et al. Arthritis Rheum 2017

Abatacept for GCA

RESULTS

- Efficacy



Relapse-free survival at 12 months

Abatacept 48%, Placebo 31% (P = 0.049)

Median duration of remission

Abatacept 9.9 months, Placebo 3.9 months (P = 0.023)

Langford et al. Arthritis Rheum 2017

Abatacept for GCA

RESULTS

- Safety

No difference in the frequency or severity of AEs including infection and serious AEs

Table 3. Serious adverse events during the study*

	Nonrandomized (n = 8)	Abatacept (n = 20)	Placebo (n = 21)
Diarrhea (3 months after abatacept)	1	–	–
Syncope, melena (3 months after abatacept)	1	–	–
Urinary tract infection (4 months after abatacept)	1	–	–
Deep venous thrombosis (6 months after abatacept)	1	–	–
Anticoagulation hematoma (6 months after abatacept)	1	–	–
Herpes zoster	–	1	–
Squamous cell carcinoma skin	–	–	1
Diarrhea/dehydration	–	1	–
Diverticulitis	–	1	–
Hyperglycemia	–	–	1
Spinal surgery	–	–	1
Syncope	–	–	1
Branch retinal artery occlusion	–	1	–
Partial vision loss	–	1	–
Retinal detachment	–	1	–
Narcotic withdrawal	–	–	1
Chronic obstructive pulmonary disease	–	–	1
Dyspnea	–	–	1
Transitional cell carcinoma	–	1	–
Endometrial carcinoma	–	1	–
Urine electrolyte disturbance	–	–	1
Knee replacement	–	1	–
Deep venous thrombosis after knee replacement	–	1	–

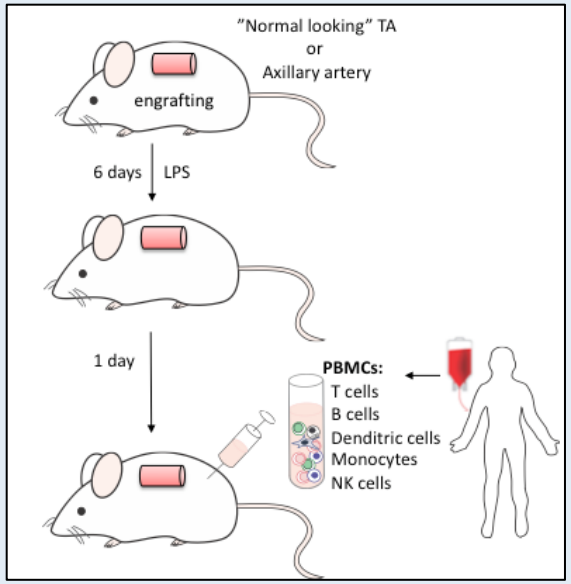
Langford et al. Arthritis Rheum 2017

JAK/STAT inhibition in GCA

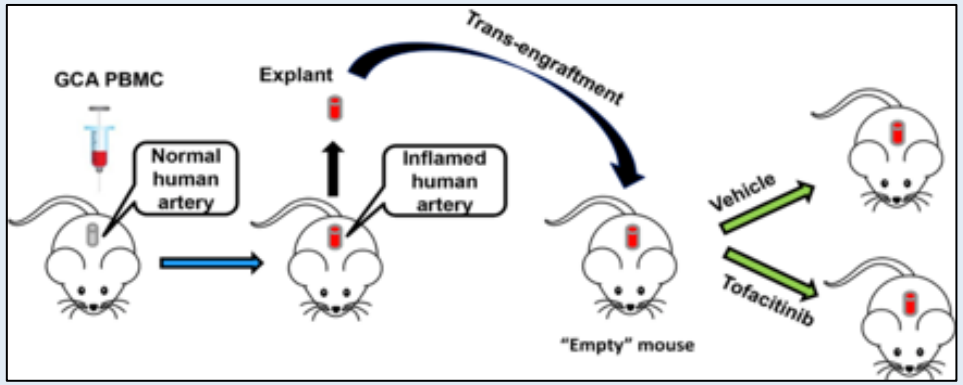
Circulation

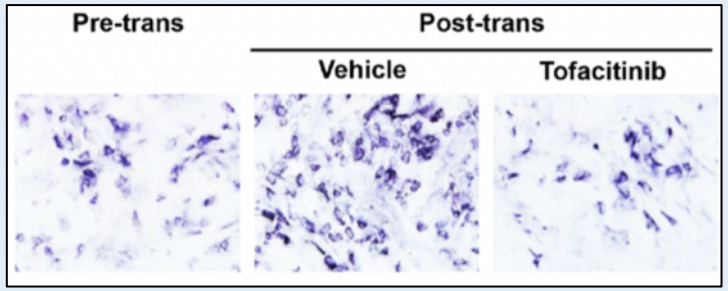
ORIGINAL RESEARCH ARTICLE

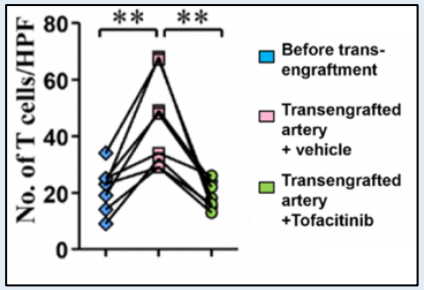
Inhibition of JAK-STAT Signaling Suppresses Pathogenic Immune Responses in Medium and Large Vessel Vasculitis



Human Artery–Severe Combined Immunodeficiency Mouse Chimeras







Ongoing JAK/STAT blockade clinical trials

- **Baricitinib** (Relapsing GCA). NCT03026504, N = 15 - Results in ACR 2021
- **Upadacitinib**. NCT03725202, N = 420 - Ongoing

Zhang et al. Circulation 2018

GM-CSF in GCA

GM-CSF

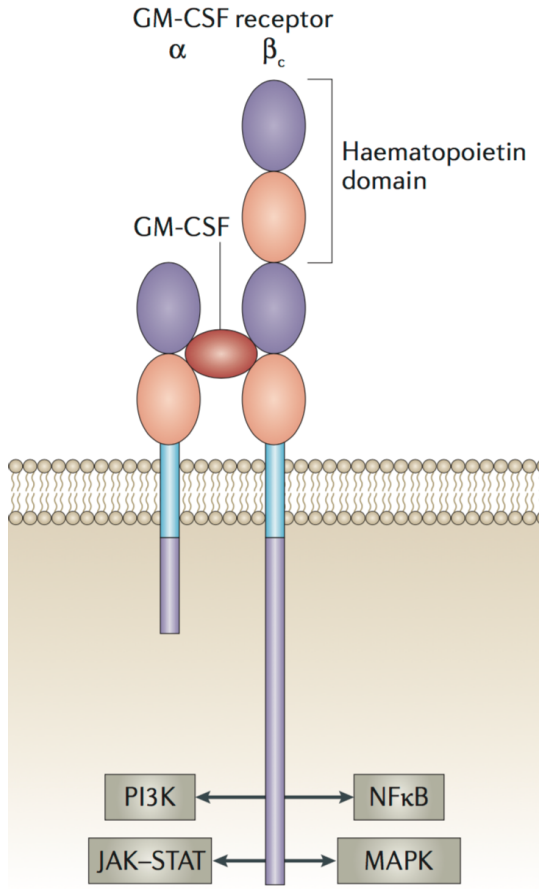
- Colony-stimulating factor (CSF) family of hematopoietic growth factors

Sources

- B and T cells
- Dendritic cells (DC)
- NK cells
- Myeloid cells (monocytes/macrophages, neutrophils)
- Tissue resident cells (endothelium, fibroblasts, VSMCs)

Functions

- Bone marrow stimulation of the myeloid linage
- DC maturation and differentiation
- Macrophage activation and function
- Myeloid-cell trafficking
- Angiogenesis
- Neutrophil priming, activation and function
- Immune response activator (IRA) B cell IgM production
- Nociception



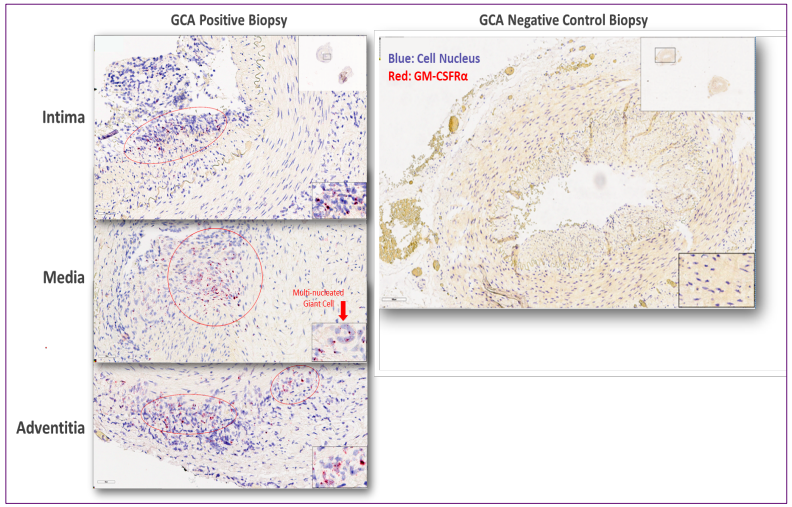
Wicks and Roberts. Nat Rev Rheumatol 2016

GM-CSF blockade in GCA - Mavrilimumab

GM-CSF at the site of inflammation

- GM-CSF, its receptor, and downstream signaling molecules are expressed by immune and endothelial cells in TAs
- GM-CSF blockade in cultured TAs resulted in decreased expression of DC, T-cell and macrophage markers
- GM-CSF blockade in cultured TAs resulted in downregulation of genes associated with the T_h1 and T_h17 immune responses (e.g., IFN-γ and IL-6)

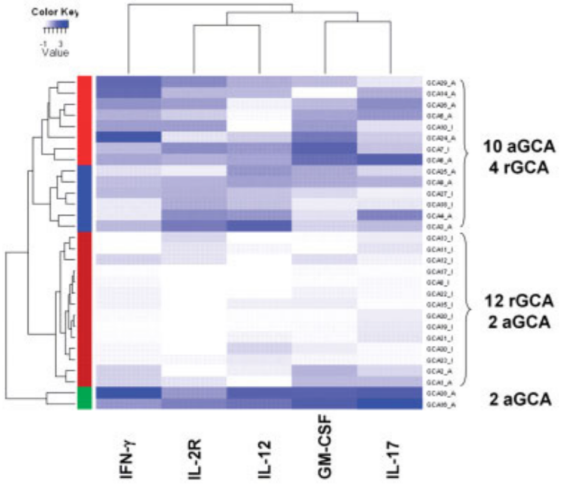
Weyand CM, et al. Ann Intern Med. 1994, Cid et al ACR 2019, Cid et al. EULAR 2020



Serum GM-CSF as a marker of disease activity

- Luminex of PBMC culture supernatants (PMA/ionomycin)
- Significantly higher GM-CSF levels in patients with active GCA compared to both patients in remission and controls
- Hierarchical cluster analysis identified a “disease activity signature” including GM-CSF, IFN-γ, IL-12, IL-17 and IL2R

Terrier B, et al. Arthritis Rheum. 2012



GM-CSF blockade in GCA - Mavrilimumab

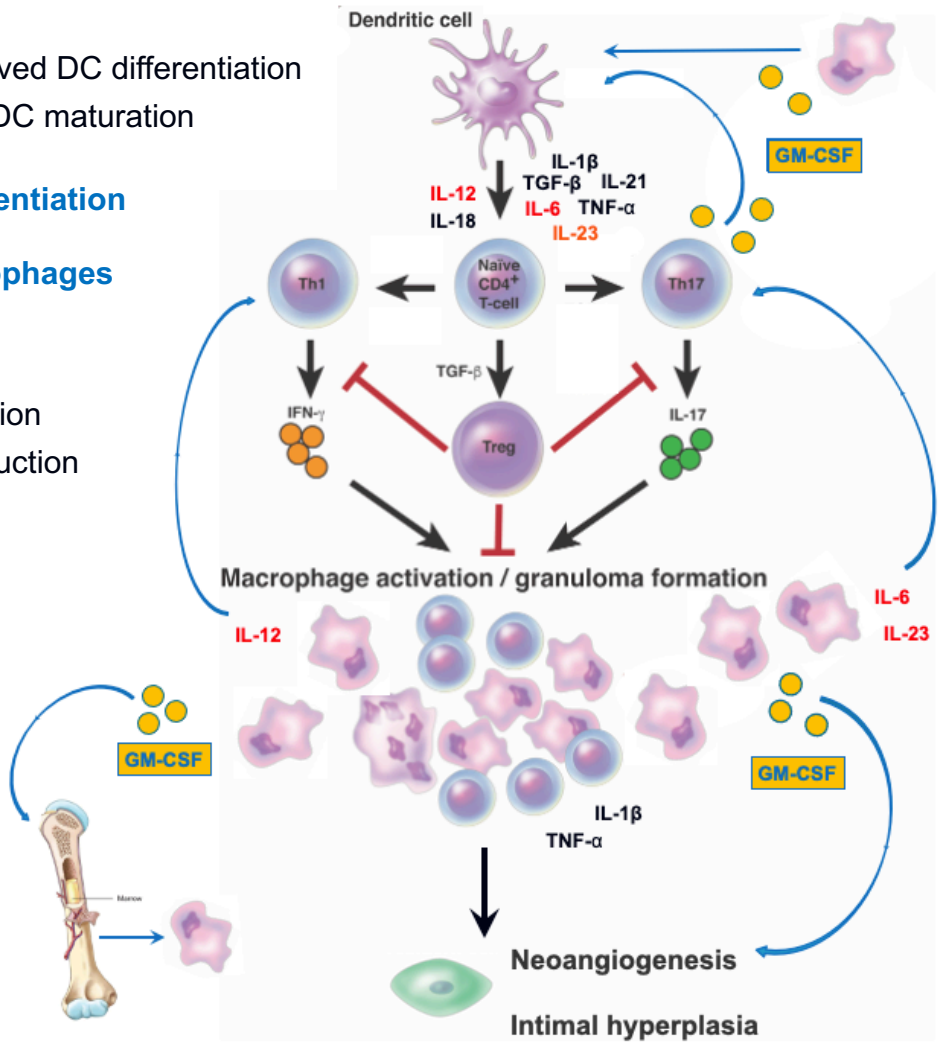
Dendritic cells

- Monocyte-derived DC differentiation
- Conventional DC maturation

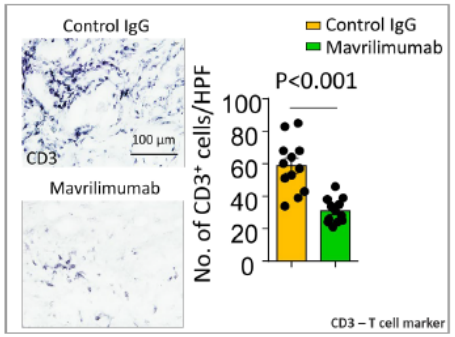
CD4 T-cell differentiation

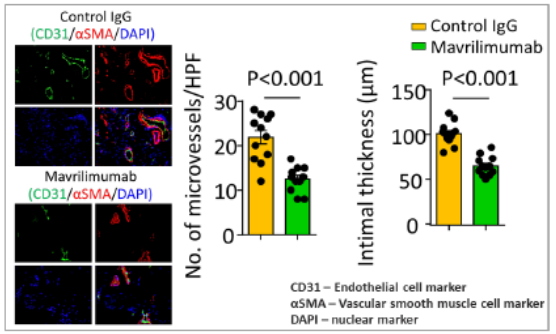
Monocyte/Macrophages

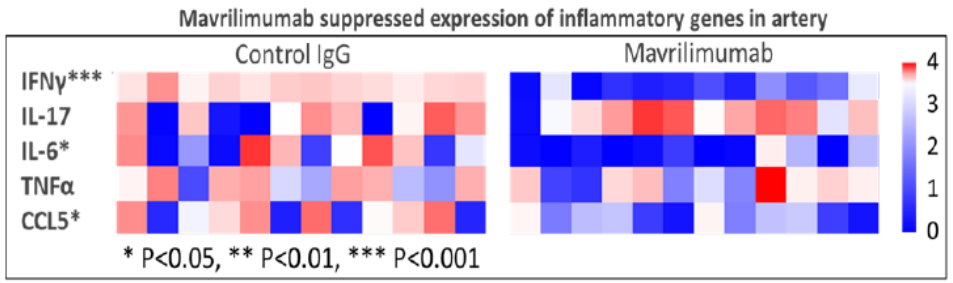
- Proliferation
- Survival
- M1 differentiation
- Cytokine production
- Trafficking



GM-CSF is pathogenic in a translational model of vasculitis





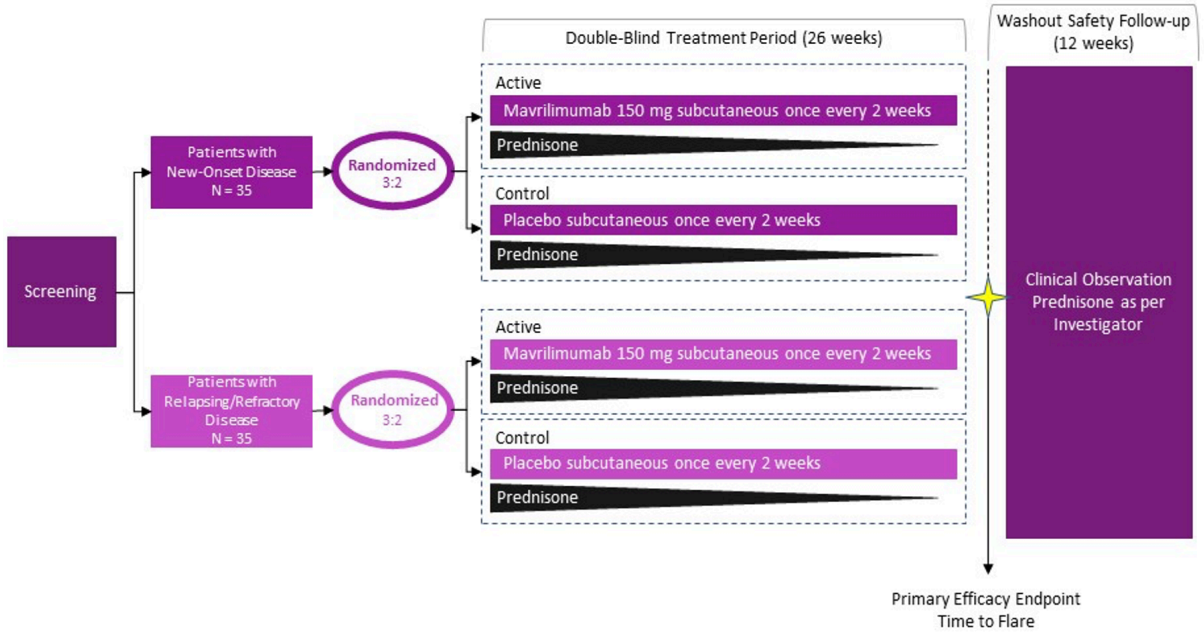


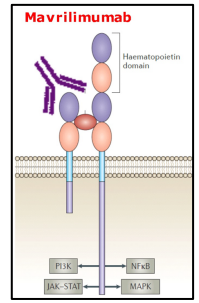
Watanabe et al. ACR 2019

Phase 2 trial mavrilimumab for GCA

DESIGN

- Phase II, randomized, double-blind, placebo-controlled trial





Study Population
- Positive temporal artery biopsy or vascular imaging
- Active disease within 6 weeks of randomization
- Glucocorticoid-induced remission by day 0

- **Primary endpoint:** Time to adjudicated flare within 26 weeks

  Definition: ESR or CRP elevation plus clinical cranial or extra-cranial manifestations or new/worsening vasculitis captured by imaging

- **Key secondary endpoint:** Sustained Remission at week 26

  Definition: absence of flare from baseline through week 26

Cid M*, Unizony S*, et al., ACR 2020. * co-principal investigators

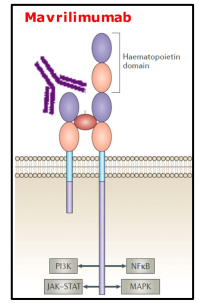
Phase 2 trial mavrilimumab for GCA

RESULTS

- Baseline characteristics

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.

Characteristic	Mavrilimumab 150 mg (N=42)	Placebo (N=28)
Age — yr, mean (SD)	69.7 (7.0)	69.7 (8.3)
Female sex — no. (%)	32 (76.2)	18 (64.3)
Race — no. (%)		
White	40 (95.2)	28 (100)
Other	2 (4.8)	0
Hispanic or Latino ethnicity — no. (%)	1 (2.4)	2 (7.1)
Weight — kg, mean (SD)	70.9 (18.7)	71.1 (12.0)
Body mass index — kg/m^2, mean (SD)	26.2 (6.8)	26.1 (3.6)
Prior treatment — no. (%)		
Glucocorticoids	42 (100)	27 (96.4)
Methotrexate	0	1 (3.6)
Diagnostic confirmation — no. (%)		
By positive temporal artery biopsy	22 (52.4)	9 (32.1)
By positive imaging	29 (69.0)	22 (78.6)
Time since diagnosis — mo, mean (SD)	7.9 (15.4)	9.8 (21.8)
Giant-cell arteritis — no. (%)		
New-onset	24 (57.1)	11 (39.3)
Relapsing/refractory	18 (42.9)	17 (60.7)
Giant-cell arteritis type — no. (%)		
Cranial signs or symptoms	32 (76.2)	21 (75.0)
Extracranial signs or symptoms	9 (21.4)	6 (21.4)
C-reactive protein level (eligibility value) — mg/dL, mean (SD)	4.7 (4.7)	3.6 (3.2)
Erythrocyte sedimentation rate (eligibility value) — mm/hr, mean (SD)	57.0 (24.6)	55.1 (30.2)
Prednisone starting dose, mean (SD)		
≤30 mg	16 (38.1)	14 (50.0)
>30 mg	26 (61.9)	14 (50.0)

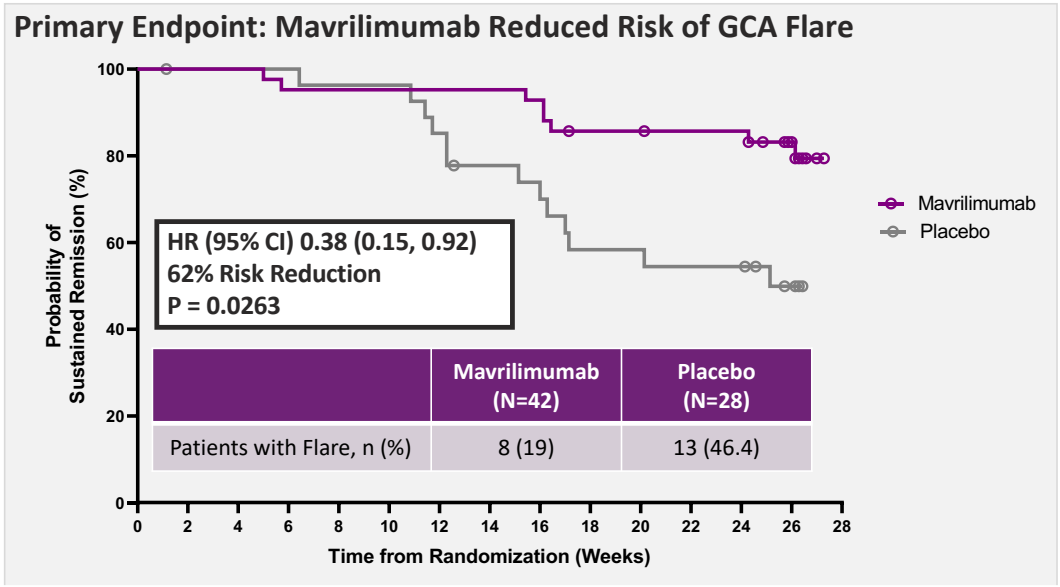


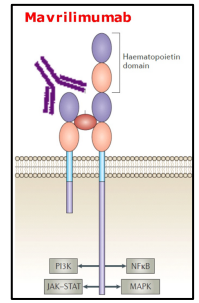
Cid M*, Unizony S*, et al., ACR 2020. * co-principal investigators

Phase 2 trial mavrilimumab for GCA

RESULTS

- Efficacy



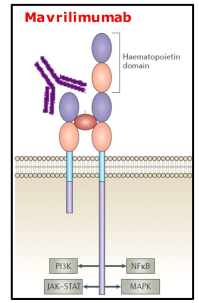


Cid M*, Unizony S*, et al., ACR 2020. * co-principal investigators

Phase 2 trial mavrilimumab for GCA

RESULTS

- Safety



	Mavrilimumab 150mg (N=42) n (%)	Placebo (N=28) n (%)
Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
By Maximum Severity [1]		
Mild	18 (42.9)	13 (46.4)
Moderate	14 (33.3)	11 (39.3)
Severe	1 (2.4)	1 (3.6)
Related to Mavrilimumab or Placebo [2]	10 (23.8)	7 (25.0)
Related to Prednisone [2]	11 (26.2)	11 (39.3)
Serious Treatment Emergent Adverse Events	2 (4.8)	3 (10.7)
Related to Mavrilimumab or Placebo [2]	0	0
Related to Prednisone [2]	0	0
Non-serious Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
Treatment Emergent Adverse Events Resulting in Death	0	0
Treatment Emergent Adverse Events Leading to Dose Interruption	1 (2.4)	2 (7.1)
Treatment Emergent Adverse Events Leading to Withdrawal of Treatment	1 (2.4)	1 (3.6)
Treatment Emergent Adverse Events of Special Interest	0	1 (3.6)

Key Points

- Rates of drug-related treatment-emergent AEs were similar across treatment groups
- No drug-related SAEs (unrelated: 2 vs 3 cases)
- No deaths, alveolar proteinosis or vision loss occurred.

Cid M*, Unizony S*, et al., ACR 2020. * co-principal investigators

GCA Guidelines

2018 EULAR

- Tocilizumab should be used in selected patients with GCA
  - ✓ Refractory or relapsing disease
  - ✓ Presence or increased risk of glucocorticoid-related adverse effects or complications

- Methotrexate may be used as an alternative to tocilizumab

Hellmich et al. Ann Rheum Dis 2018

GCA Guidelines

2021 ACR / Vasculitis Foundation

- New-onset disease: Glucocorticoids plus tocilizumab
- Relapse on moderate to high dose glucocorticoids: Add tocilizumab
- Relapse with cranial or ischemic symptoms: Add tocilizumab
- Relapse with PMR symptoms: No formal recommendations
- Active large-vessel involvement: Glucocorticoids plus tocilizumab

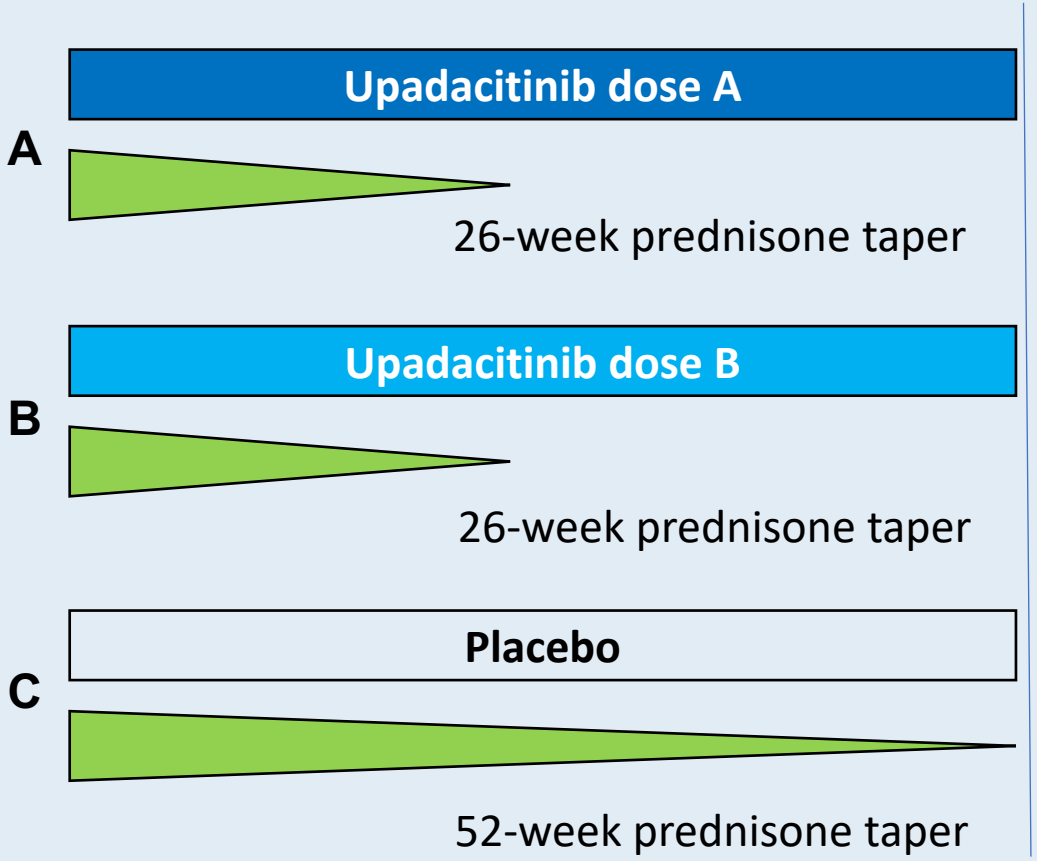
Note:

MTX or abatacept are options in case of tocilizumab inefficacy, side-effects or accessibility barriers (e.g., cost)

Maz et al. Arthritis Rheum 2021

Ongoing studies - Jakinibs

Upadacitinib - Phase 3 (N = 420)



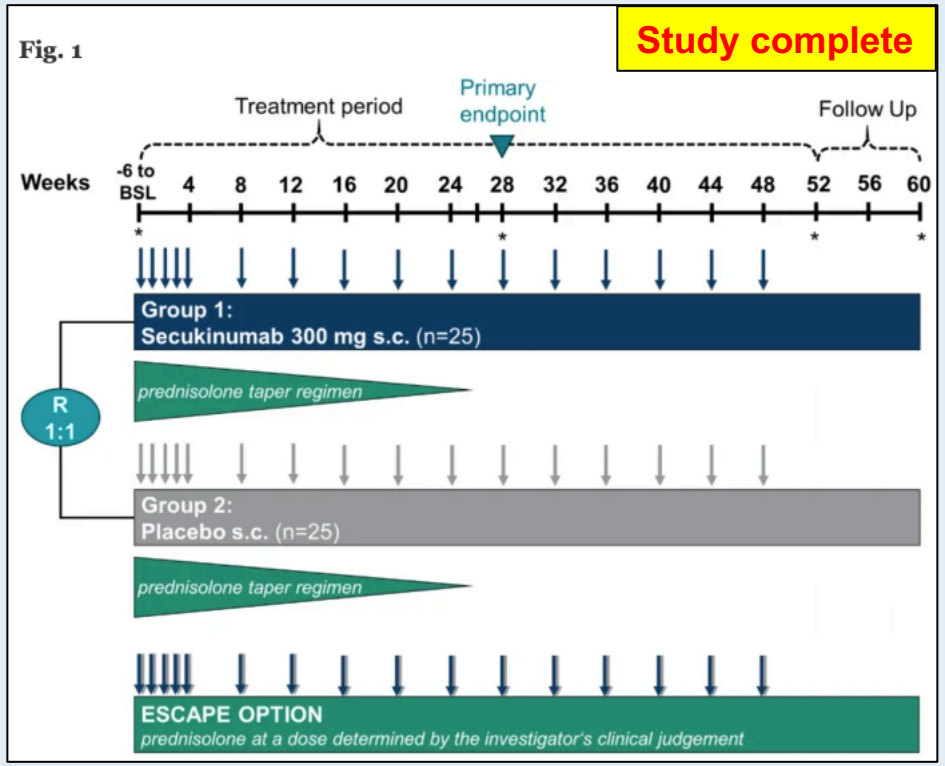
Primary endpoint

Sustained remission at week 52

ClinicalTrials.gov Identifier: NCT03725202

Ongoing studies - IL-17 blockade

Secukinumab - Phase 2 (N = 52)

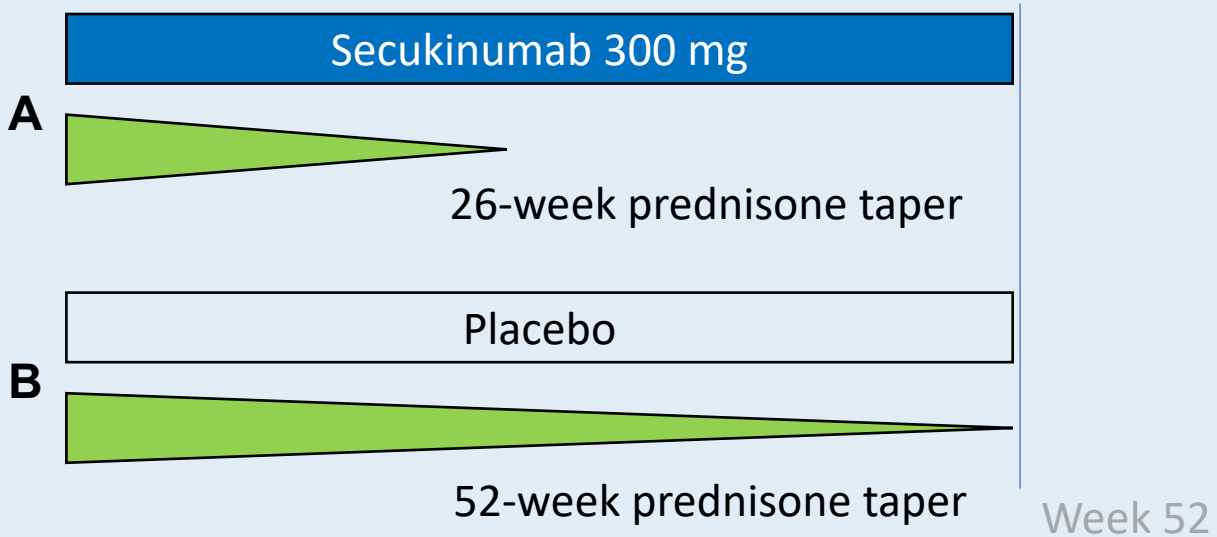


Primary endpoint

Sustained remission at week 28

ClinicalTrials.gov Identifier: NCT03765788

Secukinumab - Phase 3 (N = 240)



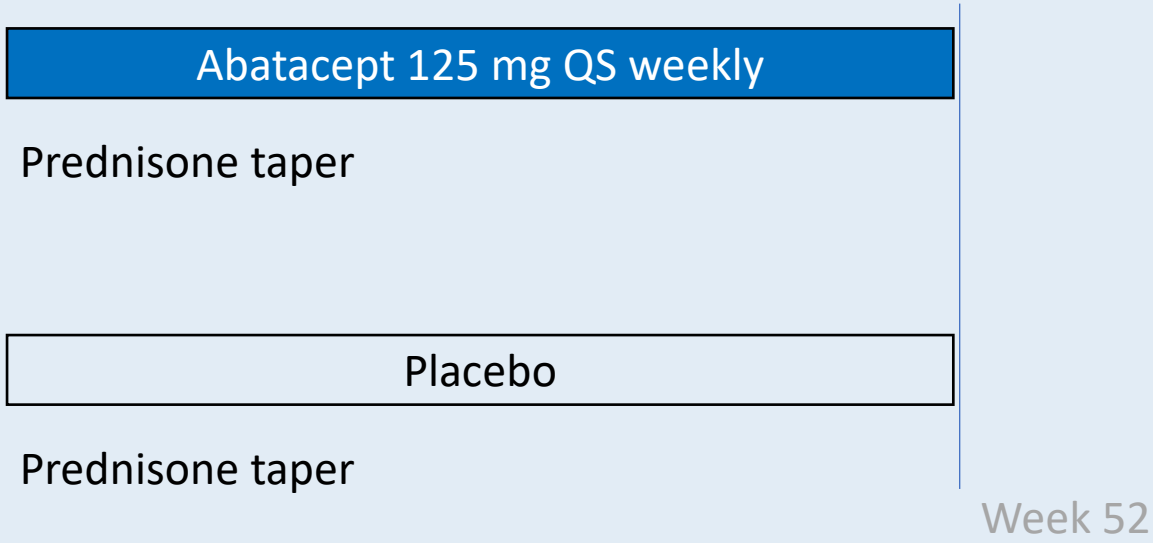
Primary endpoint

Sustained remission at week 52

ClinicalTrials.gov Identifier: NCT04930094

Ongoing studies - CD4+ T cell co-stimulation blockade

Abatacept (N = 62)



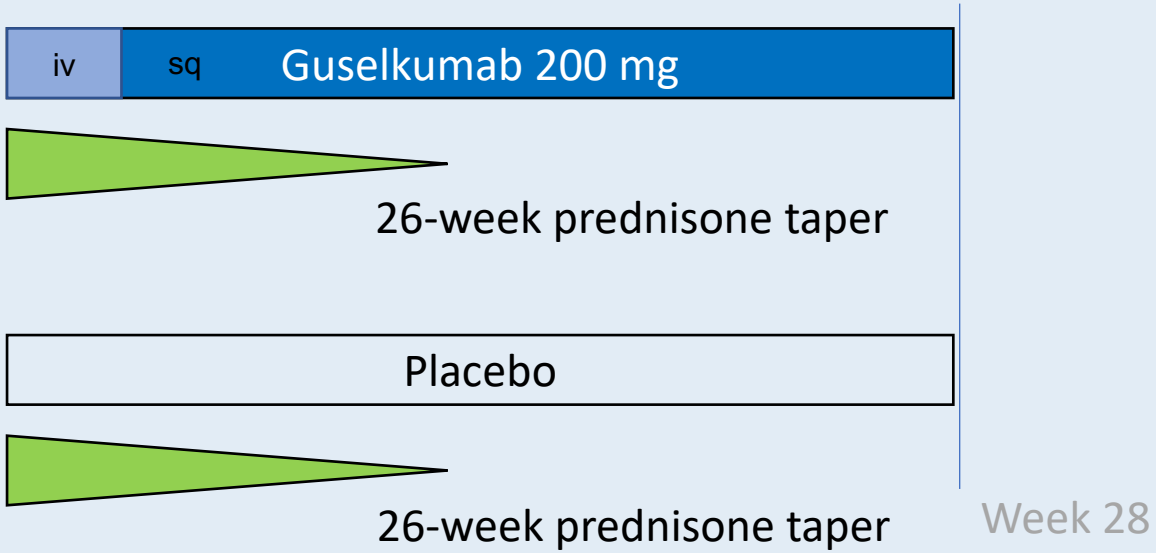
Primary endpoint

Remission at week 52

ClinicalTrials.gov Identifier: NCT03765788

Ongoing studies - IL-23 blockade

Guselkumab Phase 2 (N = 60)



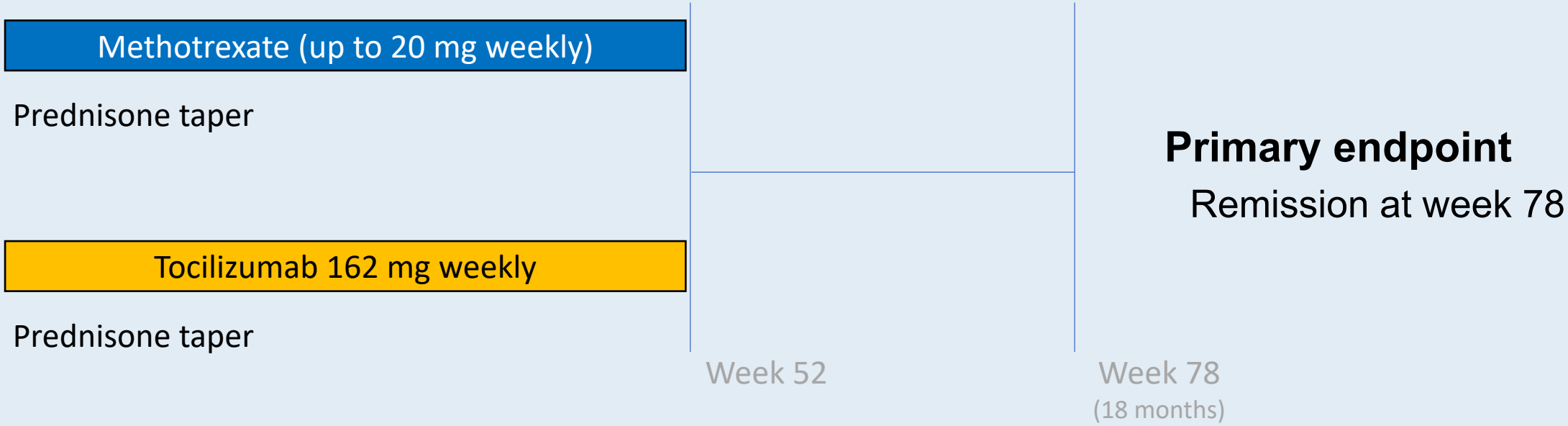
Primary endpoint

Remission at week 28

ClinicalTrials.gov Identifier: NCT03765788

Ongoing studies

Methotrexate versus tocilizumab for GCA (N = 200)



Non-inferiority design

ClinicalTrials.gov Identifier: NCT03892785

Thank you

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