Giant Cell Arteritis and Takayasu Arteritis Updates

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CME Disclosure Statements

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Unlabeled use of commercial products

To date there is one FDA approved agent for the treatment of giant cell arteritis and one approved agent for polymyalgia rheumatica

All other references to use of a commercial product for the treatment of large vessel vasculitis in this presentation constitute an unlabeled use of the product

Speaker relationship to commercial products

Provide funding for clinical research on which the speaker is an investigator

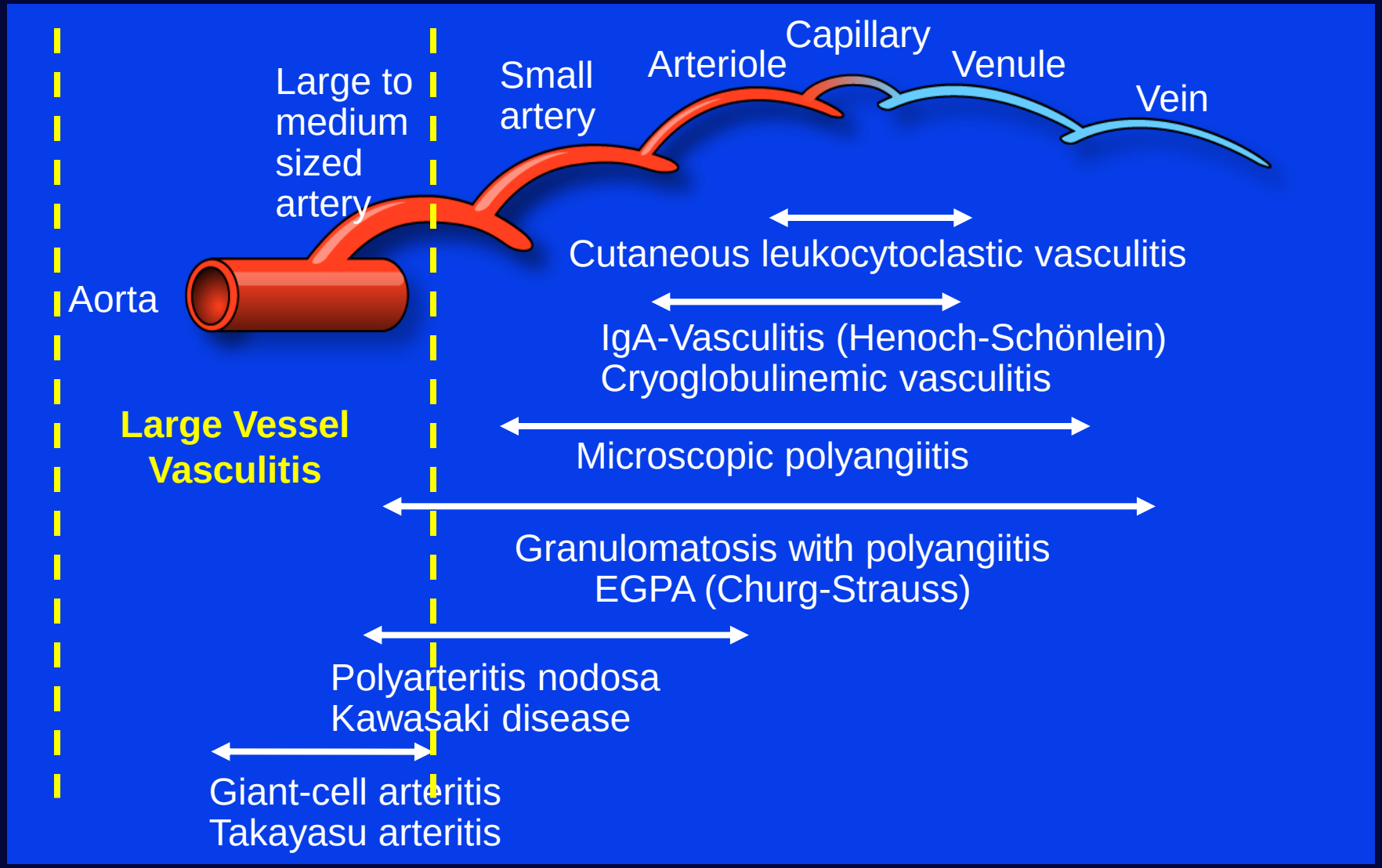
- Bristol-Myers Squibb
- GlaxoSmithKline
- AstraZeneca
- NS Pharma

Non-paid consultant: Bristol-Myers Squibb, AbbVie, AstraZeneca

Topics for Today's Discussion

- Clinical features of giant cell arteritis and Takayasu arteritis
  - Updates on imaging in large vessel vasculitis
- Treatment of giant cell arteritis and Takayasu arteritis
  - Glucocorticoids
  - Conventional immunosuppressive agents
  - Biologic agents and small molecule inhibitors
  - Non-medical management

Chapel Hill Consensus
Nomenclature of Primary Vasculitis



Jennette JC et al. Arthritis Rheum 2013; 65:1-11

Large Vessel Vasculitis: Not Just One Disease

Primary Vasculitis

Unique disease entities in which vasculitis is occurring due to an as yet unknown cause

Giant cell arteritis
Takayasu arteritis

Cogan syndrome
Behçet's disease
Kawasaki disease

Granulomatosis with polyangiitis
Microscopic polyangiitis
Polyarteritis nodosa

Isolated (focal) aortitis

Secondary Vasculitis

Vasculitis is occurring in the setting of an underlying disease or exposure

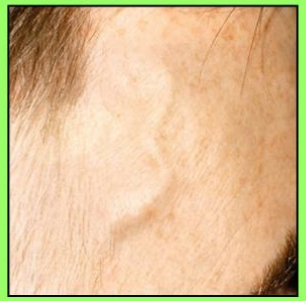
Spondyloarthropathies
Sarcoidosis
Systemic lupus erythematosus
Relapsing polychondritis
IgG4 related disease

Infection
- Syphilis
- Staphylococcus
- Salmonella
- Tuberculosis, Fungus

Trauma
Previous surgery
Atherosclerosis

Giant Cell Arteritis

- Affects people over the age of 50 (average is in the 70's), Female: Male 2:1



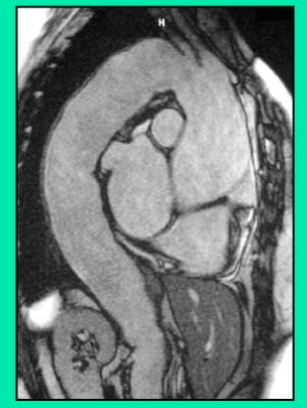
Cranial Disease

Polymyalgia Rheumatica

Giant Cell Arteritis

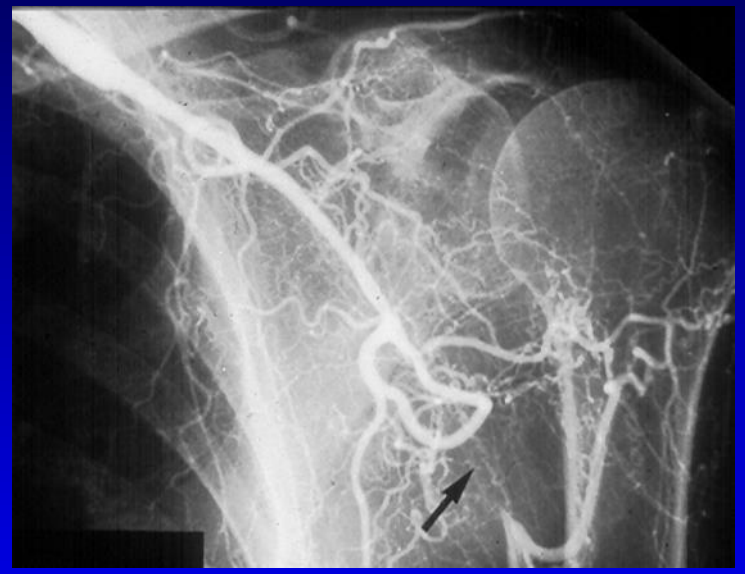
Systemic / Inflammatory Disease

Large Vessel Disease



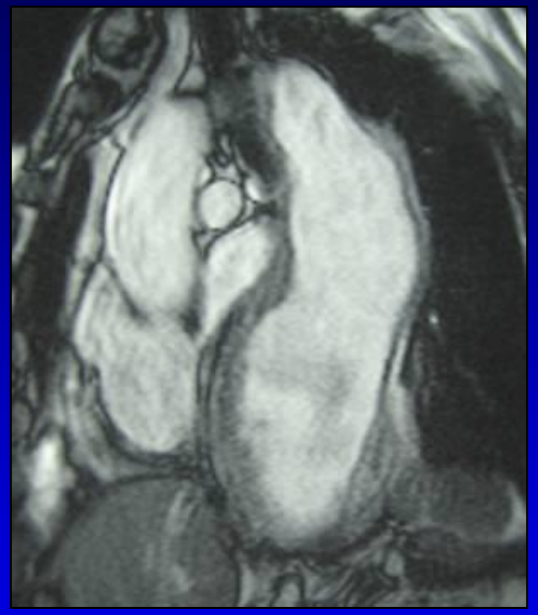
Giant Cell Arteritis - Large Vessel Disease

Subclavian Artery Stenosis



13% (1 out of every 8)

Thoracic Aortic Aneurysm



18% (1 out of every 5)

Can occur as a late manifestation

Associated with mortality

ACR / VF Guidelines:

MRA or CTA should be performed in all newly diagnosed patients with GCA to evaluate for large vessel involvement

Maz et al. A&R 2021;73:1349

Evans et al. Ann Int Med 1995;122:502

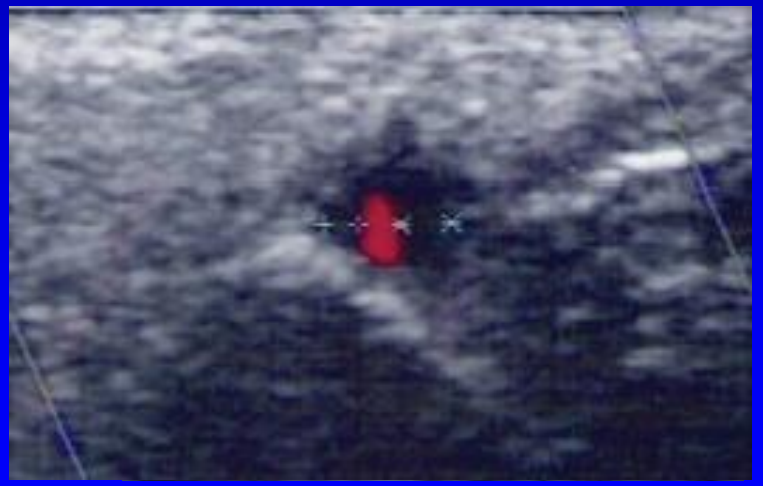
Nuenninghoff et al. A&R 2003; 48:3522

Giant Cell Arteritis
Utility of Ultrasound

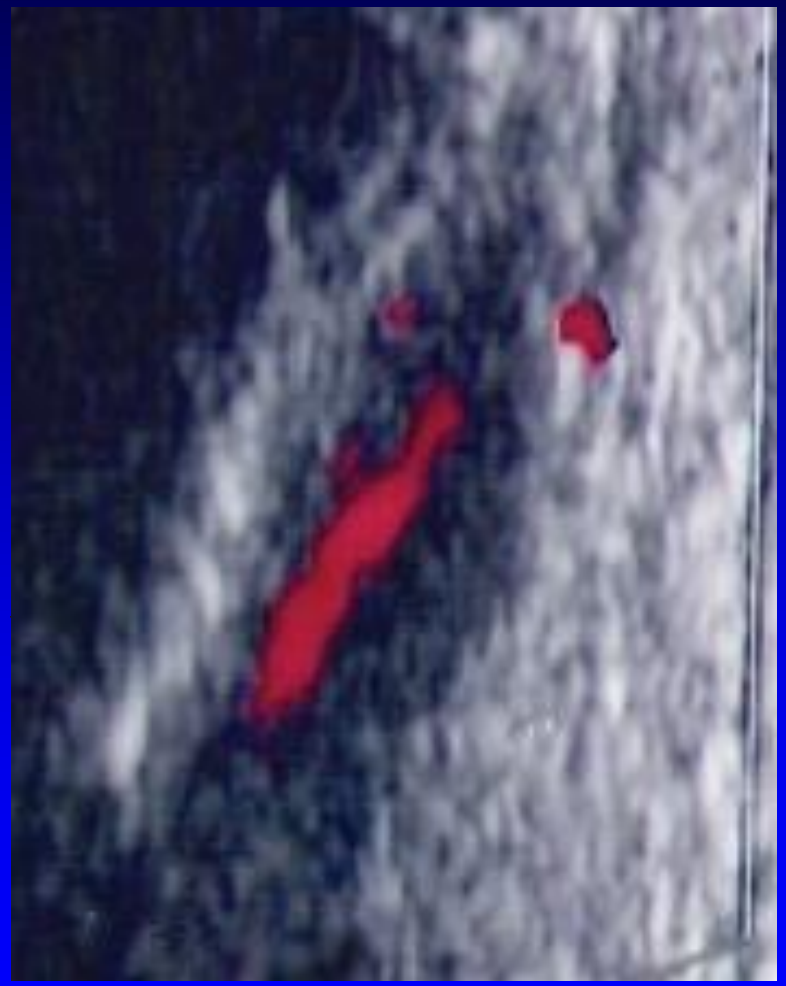
Color Duplex Ultrasonography

Hypoechoic Echo

Corresponds to a dark area
around the lumen of an inflamed artery



Transverse section



Longitudinal section

Karahaliou et al. Arth Care and Res 2006;8(4):R116

Giant Cell Arteritis
Utility of Ultrasound

Schmitt et al. NEJM 1997;337:1336

- 73% of GCA and 0% controls had a halo around the lumen of the temporal artery
- In patients with typical features and halo, biopsy may not be necessary

Salvarani et al. Ann Internal Med 2002;137:232

- Halo did not improve diagnostic accuracy beyond physical exam

Many studies followed, showing US had potential utility in GCA but was also user dependent

EULAR LVV Imaging Recommendations *(Dejaco et al. ARD 2018;77:636, Duftner et al. RMD Op 2018)*

- Ultrasound of temporal ± axillary arteries is recommended as the first imaging modality in patients with suspected predominantly cranial GCA. “Ultrasound provides a high diagnostic value for cranial GCA”

ACR/EULAR Classification Criteria for GCA *(Ponte et al. A&R 2022;74:1881)*

- (+) halo sign on temporal artery US had equal scoring to a (+) temporal artery biopsy

Use of ultrasound in diagnosis must be determined on a site-to-site basis

Giant Cell Arteritis

Temporal Artery Magnetic Resonance Imaging (MRI)

Klink et al. Radiology 2014; 272:844

- 98 patients - MRI sensitivity 89%, specificity 75%

Rhéaume et al. A&R 2017; 69:161

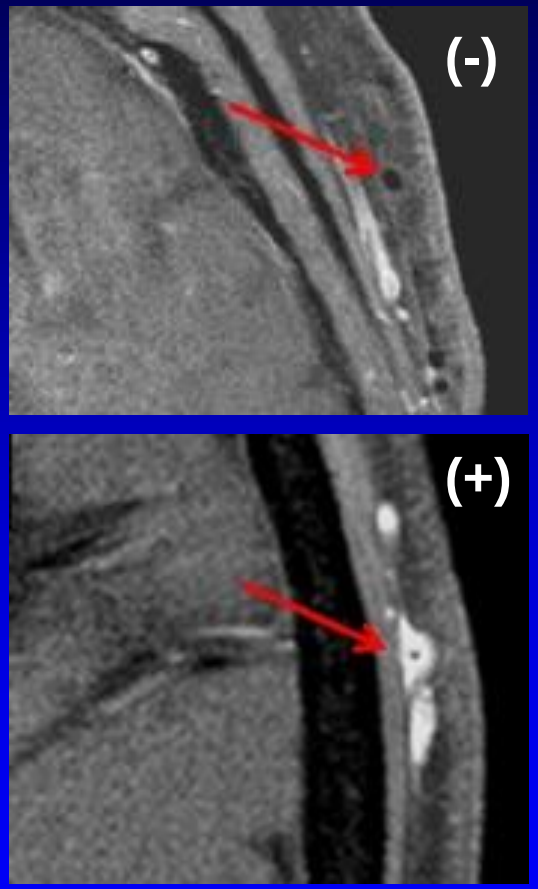
- 171 patients - 3T MRI and temporal artery bx
- MRI sensitivity 94%, specificity 78%
- Negative predictive value of MRI 98%
- Normal MRI strongly associated with a (-) bx

Rhee et al. ACR Open Rheumatol 2024;6:189

- Orbital MRI can evaluate multiple structures informative in GCA: ocular vessel wall, orbital muscles

Limitations of temporal artery/orbital MRI

- Cost, availability, radiologic expertise with MRI
- Potential to be affected by prednisone treatment



Cranial artery / orbital MRI may have utility in selected settings

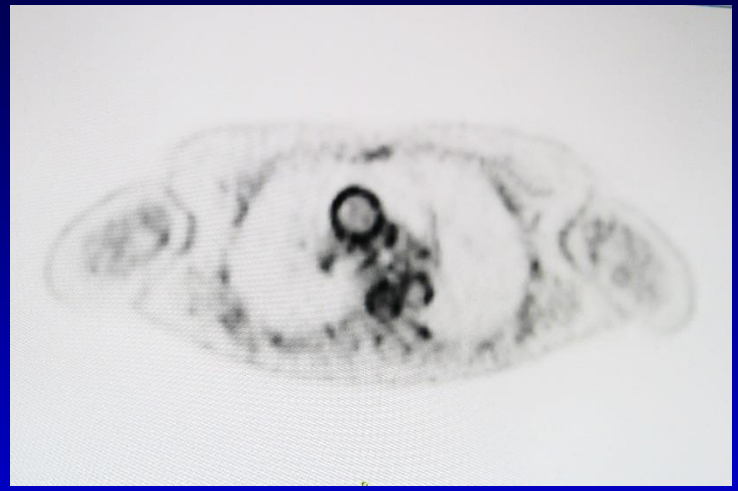
Large Vessel Vasculitis
Positron Emission Tomography (PET)

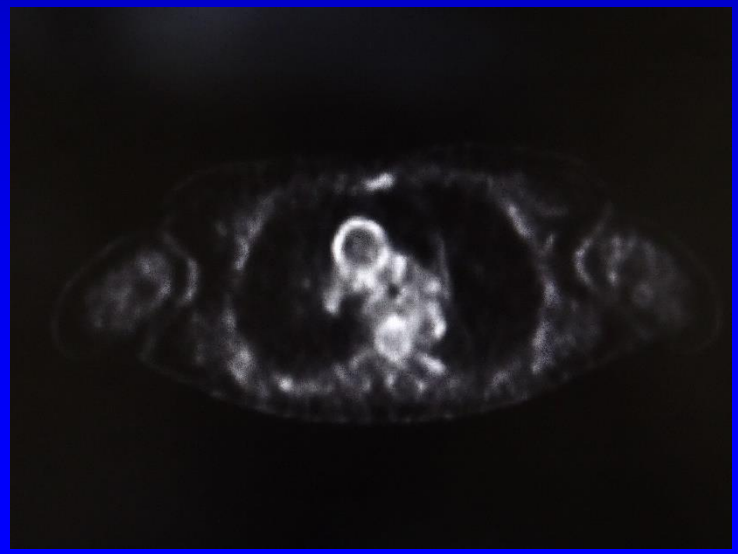
Utilizes radiolabeled fluorodeoxyglucose (FDG)
to visualize metabolically active tissue

Uptake in large vessels was first
demonstrated in GCA when looking for cancer
in patients with constitutional symptoms

Blockmans et al. Rheumatol 1999;38:444

Utility of PET in large vessel vasculitis has
continued to raise many questions





Large Vessel Vasculitis
Positron Emission Tomography (PET)

Moreel et al. Ann Int Med 2023;176:1321

- Association of vascular FDG uptake at diagnosis and later change in thoracic aortic dimensions
  - 106 patients with GCA and PET imaging 3 days or less after initiation of glucocorticoids
  - CT imaging yearly for a maximum of 10 years
  - PET scans were scored 0 to 3 in 7 vascular areas and summed to a total vascular score (TVS)
  - PET scan results were positive when FDG uptake was grade 2 or greater in any large vessel
  - Those with a positive PET had a greater increase in the diameter of the ascending aorta
  - Higher TVS was associated with greater yearly increase in thoracic aortic dimensions

Conclusion and questions:

- Performing PET at diagnosis may help to estimate the risk for aortic aneurysm formation
- Limitation: obtaining PET within the $\leq$ 3 days of starting glucocorticoids as in this study is difficult
- PET (-) does not rule out the potential for aneurysm development – monitoring remains important

Large Vessel Vasculitis
Positron Emission Tomography (PET)

Grayson et al. A&R 2018; 70:439

- LVV PET sensitivity 85%, specificity 83%, vessel uptake was seen in some cases of atherosclerosis
- PET in active disease versus remission - Activity seen in 58% of those in clinical remission
- PETVAS score (assessment of uptake in 9 locations) – relapse more common with higher score

Quinn et al. A&R 2023;75:98

- Examined arteriographic progression on MRA/CTA and if PET activity predicts progression
  - 1091 arterial territories in 70 patients (TAK=38, GCA=32) over 1.0-2.7 years
  - 30 territories (2.7%) in 16 patients had changes between studies - all stenotic, all TAK, all symptomatic
  - 80% with new changes had PET activity at baseline
  - Of those with PET activity at baseline – only 8% developed arteriographic change in that location

Quinn et al. A&R 2024; 76 (suppl 9).

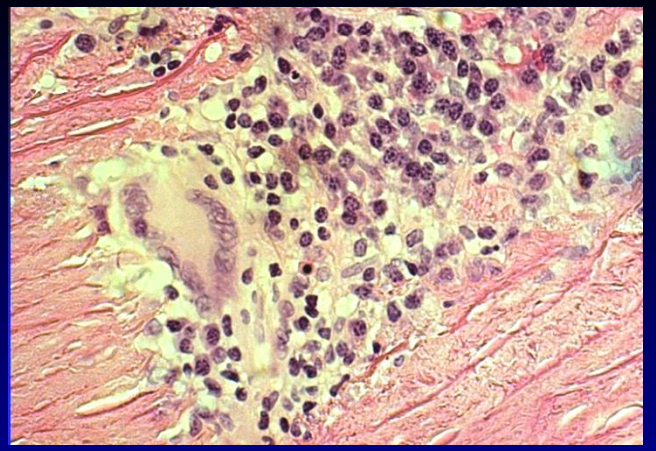
- 36 patients with GCA receiving tocilizumab underwent PET - PET has limited value to guide treatment decisions or inform relapse risk when obtained during clinical remission in patients receiving tocilizumab

Utility of PET in serial follow-up after diagnosis remains is unclear

Takayasu Arteritis

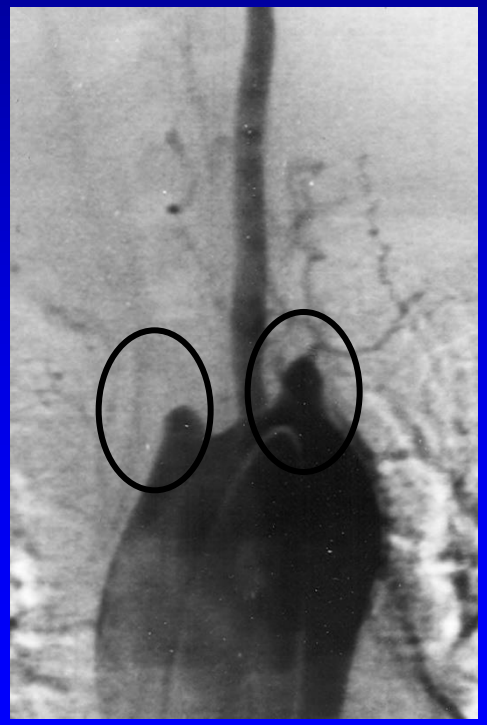
Large vessel granulomatous vasculitis

More common in women
Age 15-45 years

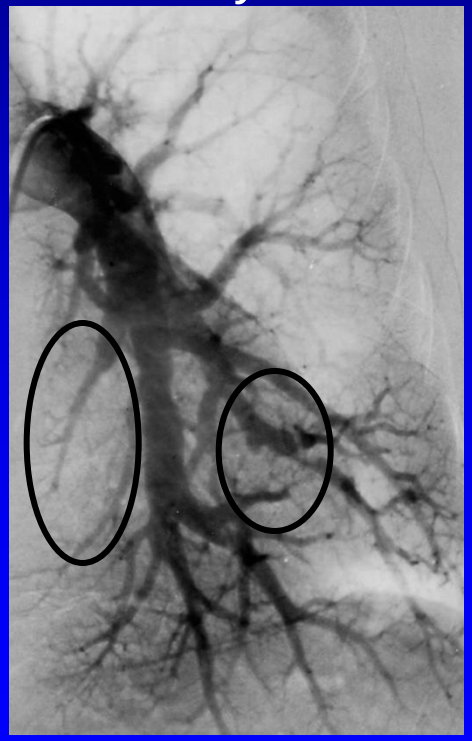


Aorta

Main branches



Pulmonary arteries



Kerr et al. Ann Intern Med 1994; 120:919

Takayasu Arteritis

Distribution of Vascular Lesions

Vessel (%)	North America[1]	India[2] Age onset ≥ 16 yrs	India[2] Age onset ≤ 16 yrs	Symptoms / Signs
Subclavian	76	58	49	Arm claudication
Carotid	57	37	22	TIA, stroke, syncope, vision
Renal	20	36	54	Hypertension
Iliac	16	6	6	Leg claudication
Sup. Mesenteric	34	25	33	Abdominal angina (rare)
Thoracic Aorta	27	28	28	CHF (aortic root)
Abdominal Aorta	28	39	51	Aneurysm: Often no symptoms Stenosis: claudication

1. *Quinn et al. Sem Arth Rheum 2020;50:576*
2. *Danda et al. Rheumatol 2021;60:2246*

Takayasu Arteritis

Diagnosis - Imaging

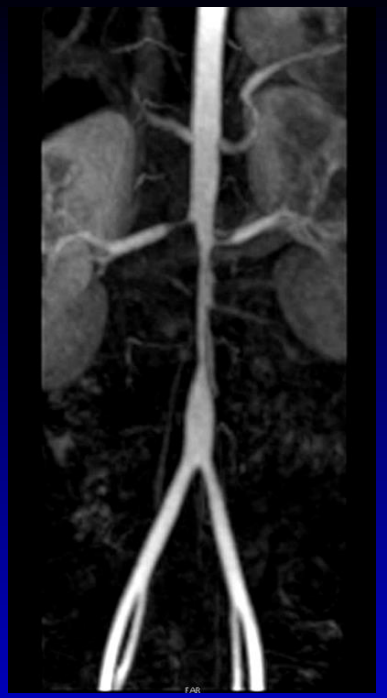
Important to image the entire aorta and its branch vessels at diagnosis

Why ?

- Support diagnosis — number, location of lesions can narrow differential
- Anticipate problems — knowledge of asymptomatic lesions in critical locations (CNS, renal) can guide monitoring
- Detect new disease — with knowledge of baseline anatomy, new lesions in new territories can be detected on follow-up

Takayasu Arteritis

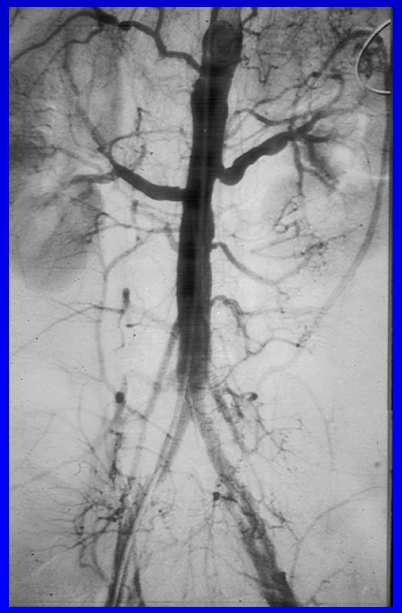
Arteriographic Imaging Modalities



CTA or MRA are used almost exclusively in diagnosis and follow-up

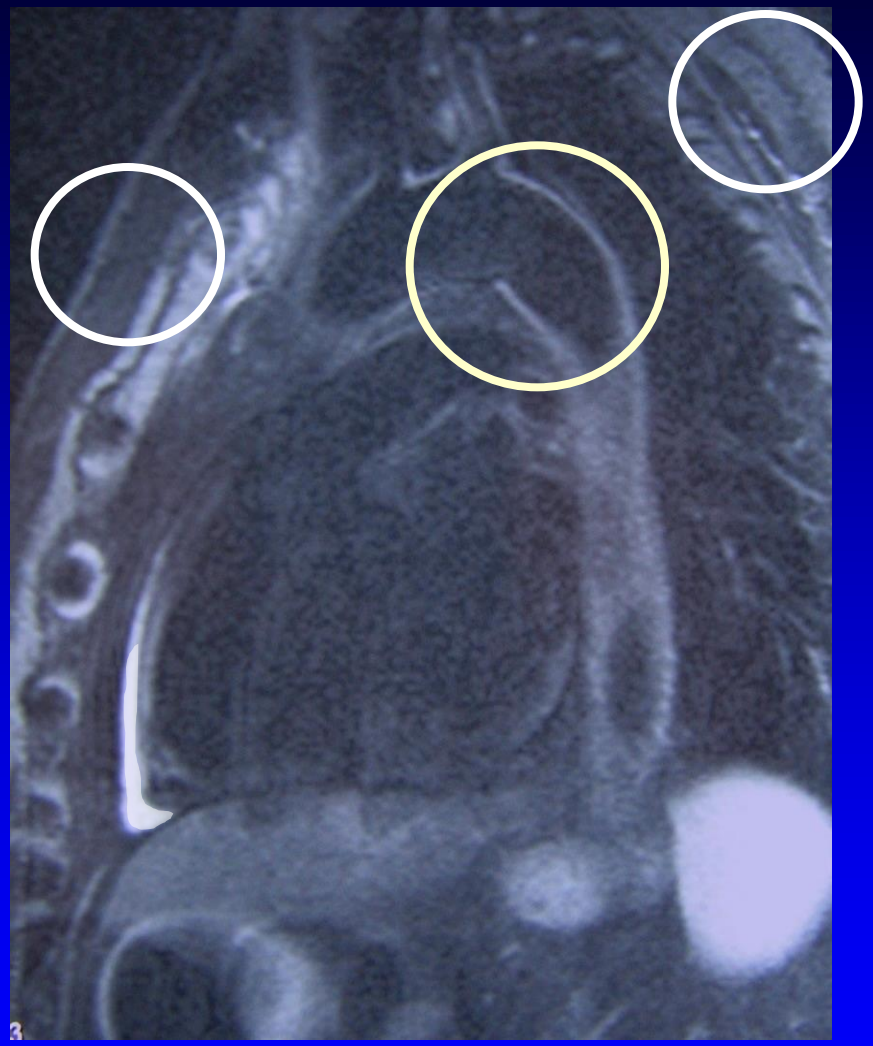
- Non-invasive
- No risk of bleeding or embolism

In what settings should a catheter-directed dye arteriogram be considered ?



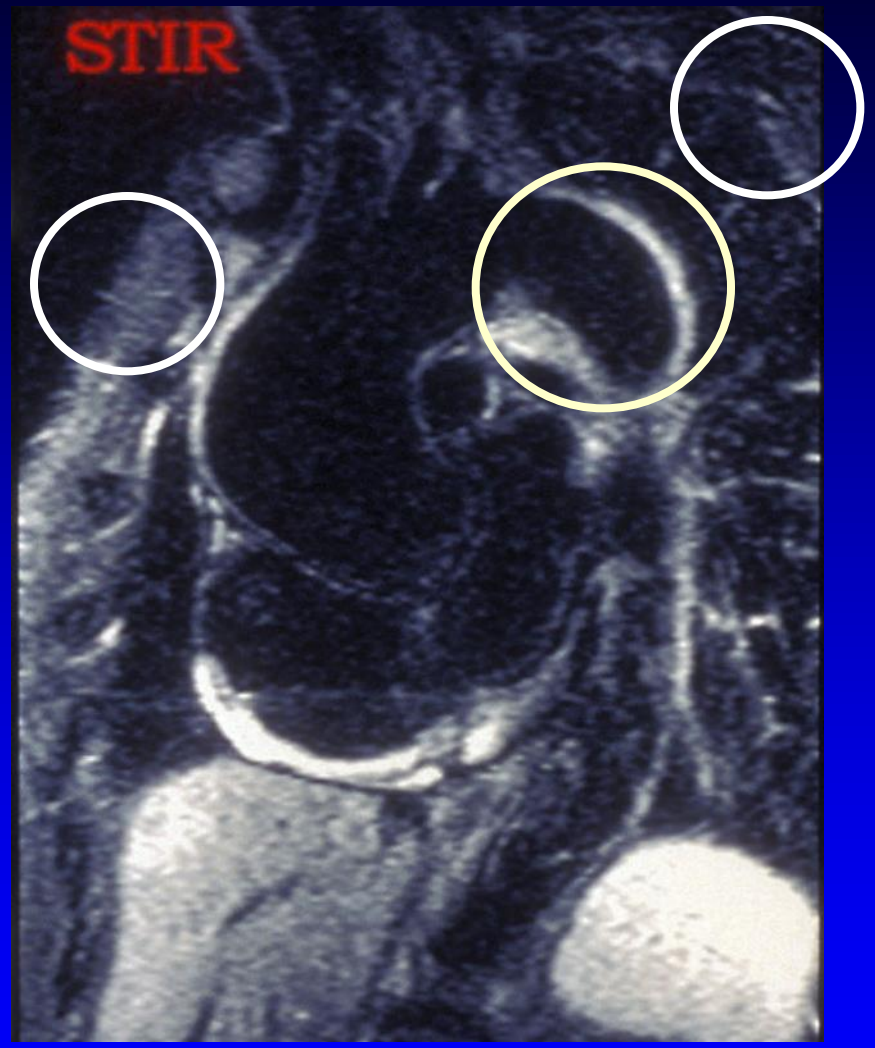
- Abnormal cardiac functional study (coronary arteriography)
- When central blood pressure measurement is needed (stenoses all extremities)
- Uncertain abnormality or change on CTA/MRA that would impact therapy
- Diagnostic dilemmas
- Need to evaluate medium-sized vessels

Magnetic Resonance to Assess the Vessel Wall



Isointense compared to muscle

No Edema



Hyperintense compared to muscle

Edema – (? Inflammation ?)

Takayasu Arteritis

MR Imaging to Assess Disease Activity

Tso et al: Arthritis Rheum 2002;46:1634

Vessel wall edema seen in:

- 94% active disease
- 56% apparent clinical remission

60% had vessel hyperintensity by MR for > 2 years without new vascular lesions

Enhancement may not always = active inflammation

Raises doubts about utility of MRI edema to assess disease activity

Takayasu Arteritis and Giant Cell Arteritis

Relationship

Are Takayasu arteritis and Giant cell arteritis related diseases ?

Unknown

Similarities:

- Involvement of large vessels
- Histologic evidence of granulomatous inflammation

Differences:

- Age of involvement
- Distribution of vessel involvement
- ? Treatment response

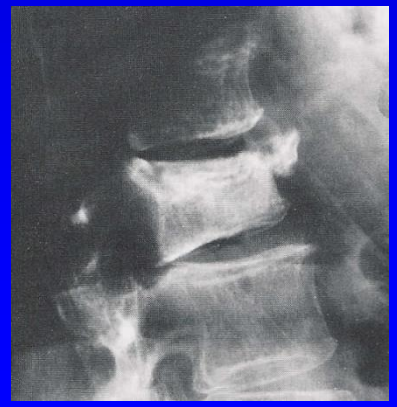
Differences in response to treatment has raised interesting questions

Maksimowicz-McKinnon K et al. Medicine 2009;88:221

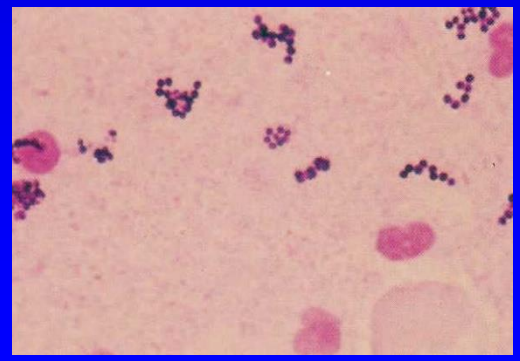
Giant Cell Arteritis
Treatment with Glucocorticoids

- Compelling evidence that glucocorticoids protect vision
  - *Shick et al. Proc Mayo 1950;25:492* - 1st use of glucocorticoids in GCA
  - *Birkhead et al. JAMA 1957;163:821* - B/L blindness went from 17% to 9%
  - *Aiello et al. Opth 1993;100:550* - 1% probability of visual loss after starting
- Relapse rate from prospective trials: 75-90%
- Treatment length: typically over 2 years, for some is over 4

Glucocorticoids are effective but do not prevent relapse and long durations are required in most patients



Problem – Toxicity (up to 86%)



Giant Cell Arteritis
Treatment – Methotrexate (MTX)

- *Jover et al. Ann Int Med 2001;134:106, Hoffman et al. A&R 2002;46:1309*
  - 2 randomized trials
  - Largest study showed no difference in relapse or prednisone exposure

- Meta-analysis *(Mahr et al. A&R 2007; 56:2789)*
  - Have to treat 11 patients with MTX to prevent a cranial relapse
  - MTX use was associated with a reduction in cumulative prednisone dose
  - MTX did not reduce frequency of prednisone side effects
  - MTX provided at best a very modest effect in GCA

Does not support the routine use of methotrexate in GCA

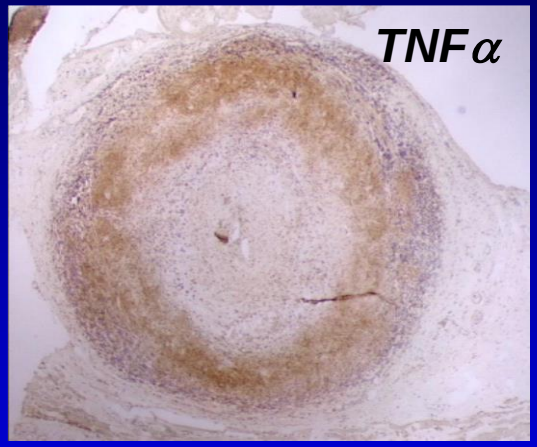
(Also a negative study in PMR *Caporali et al, Ann Int Med 2004;141:493)*

Giant Cell Arteritis - Potential Disease Mechanisms

Evidence that GCA is an antigen driven disease

Macrophages - Dendritic cells - T lymphocytes

Evidence of tissue production of
pro-inflammatory cytokines
(TNFα, IL-6) in temporal arteries



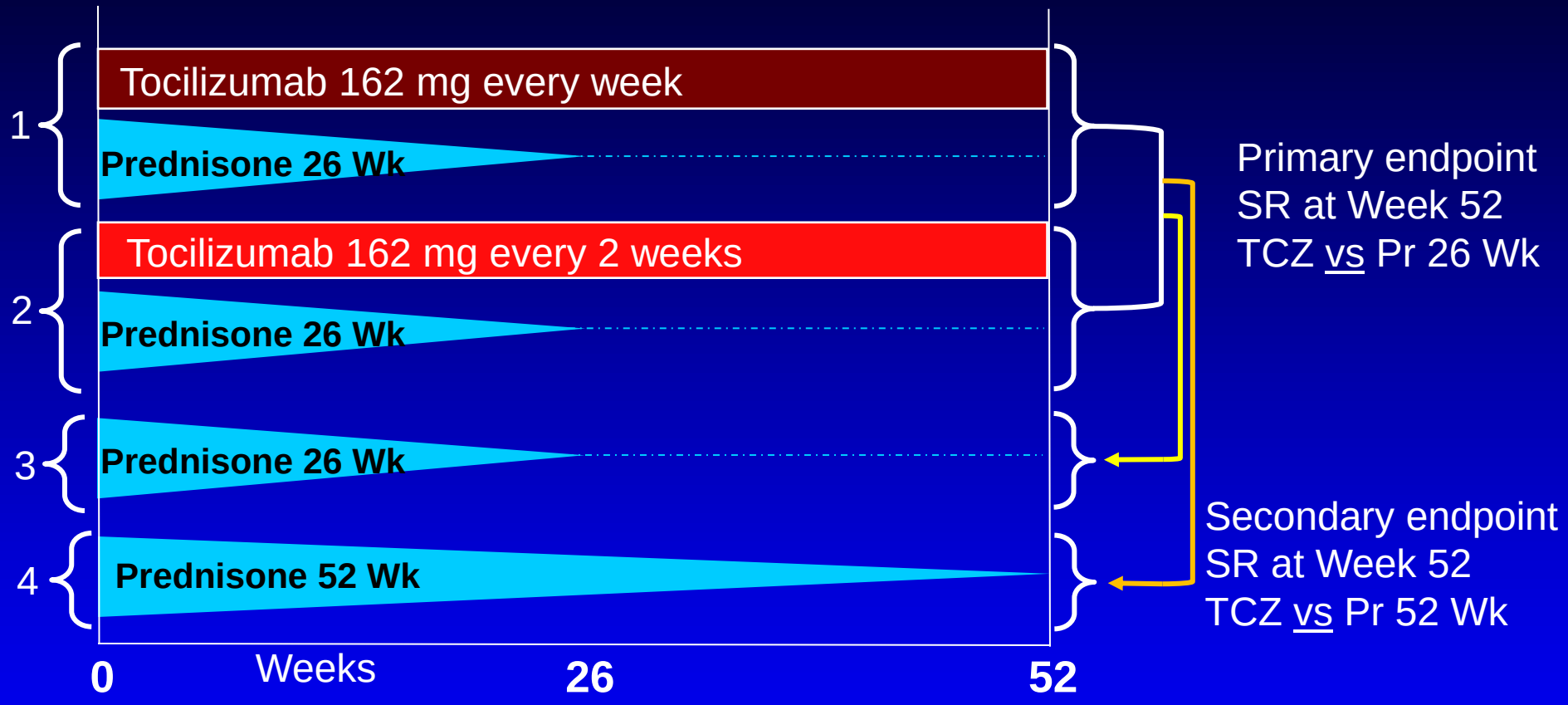
TNF inhibitors

- *Hoffman et al. Ann Intern Med 2007; 146:621*
  - Randomized trial prednisone + infliximab 5 mg/kg every 8 weeks of placebo
  - Infliximab did not increase proportion relapse free at week 22 (p=0.651)
  - Infliximab associated with an increased risk of infection
- *Seror et al. ARD 2014;73:2074* – negative trial with adalimumab
- *Salvarani et al. Ann Int Med 2007;146:631* – negative trial of infliximab in PMR

There is no role for TNF inhibitors in the treatment of giant cell arteritis

Phase 3 Randomized Trial of Tocilizumab in Giant Cell Arteritis

Stone et al. NEJM 2017;377:317



- Initial prednisone dose 20-60 mg/day - chosen by investigator
- Prednisone doses were double-blinded at < 20 mg/day (indicated by – · – · –)
- Remission: no symptoms + normal ESR and CRP
- Sustained remission (SR): no flare after week 12 + completion of pred taper

Phase 3 Randomized Trial of Tocilizumab in Giant Cell Arteritis

Stone et al. NEJM 2017;377:317

Treatment group (Randomized 2:1:1:1)	Pred 26 Wk N=50	Pred 52 Wk N=51	Weekly TCZ N=100	Every other Wk TCZ N=50
SR week 52	14%	18%	56%	53%
TCZ vs Pred 26 Wk (Primary)			42 (P< 0.001)	39 (P< 0.001)
TCZ vs Pred 52 Wk (Secondary)			38 (P< 0.001)	35 (P< 0.001)
Median total pred dose (range)	3296 (932-9778)	3818 (822-10,698)	1862 (630-6602)	1862 (295-9912)
Adverse events	96%	92%	98%	96%
Serious adverse events (SAE)	22%	25%	15%	14%
Infection SAE	4%	12%	7%	4%

- Enrolled 251 newly diagnosed or relapsing patients with GCA
- Similar rates of SR in prednisone arms
- Both tocilizumab arms were superior to either 26-week or 52-week prednisone taper
- Tocilizumab associated with a lower cumulative prednisone exposure (wide range)
- Adverse events balanced across groups, no bowel perforations
- SR with tocilizumab every week was only 56%

Further Insights from the Phase 3 Randomized Trial of Tocilizumab in GCA

Stone et al. A&R 2019; 71:1329, Stone et al. Rheumatol 2022;61:2915, Stone et al. Lancet Rheumatol 2021;3;e328

- Most flares occurred while patients were still on prednisone
  - TCZ-treated: 64% of flares occurred while still on prednisone (median 2 mg/day)
  - Flares on prednisone > 10 mg/day: TCZ 25% of flares, prednisone-alone 22% of flares

- Tocilizumab every week vs every other week
  - Both effective in newly diagnosed but only every week was effective in those enrolled at relapse
  - Every week had longer time to first flare after treatment stopped

- Over half of patients who were in remission relapsed when TCZ was stopped after 1 year
  - TCZ every week - 42% maintained TCZ-free and glucocorticoid–free remission (58% relapsed)
  - TCZ every other week - 29% maintained TCZ-free and glucocorticoid-free remission (71% relapsed)

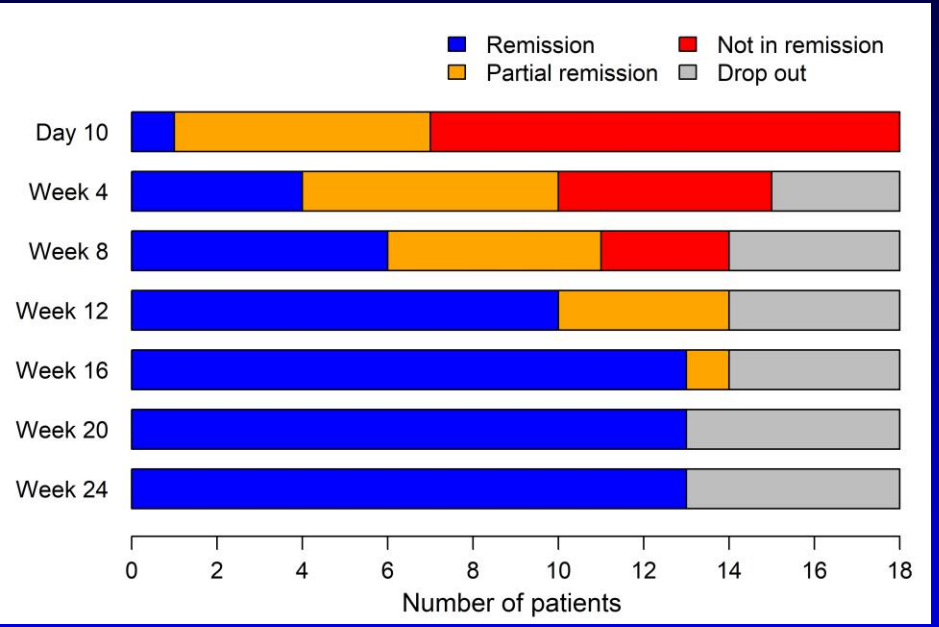
The published experience supports the effectiveness of tocilizumab in GCA

Either SC 162 mg/week or intravenous 6 mg/kg/month (*Schmitt C, et al. Art Res Ther 2022;24:133)*

There remains concerns for sustained remission, relapse, and toxicity

Tocilizumab and Shorter Course Glucocorticoids

- *Christ et al. Lancet Rheumatol 2021;3:e619*
  - Open-label study, 18 patients, newly diagnosed GCA
    - IV methylprednisolone 500 mg/day x 3 days (only GC) + TCZ 8 mg/kg IV x 1 then 162 mg/week SC Day 10-Week 52
  - Did not meet primary endpoint
    - 14 achieved remission - slow onset (mean 11 weeks)
    - 3 were non-responders - including one with visual loss
    - 1 withdrawn with severe hepatotoxicity
  - Does not support use of “ultra-short” glucocorticoids



- *Unizony et al. Lancet Rheumatol 2023;5:e736*
  - Open-label study, 30 patients – new diagnosis or relapsing
    - Tocilizumab 162 mg/week SC x 52 weeks + 8-week prednisone taper (initial doses varied)
  - 100% remission within 4 weeks. No episodes of vision loss
  - 23 (77%) sustained prednisone-free remission at Week 52, 7 (23%) relapsed, median 15.8 weeks

Using prednisone courses of < 26 weeks with tocilizumab may warrant further study but should not be routinely used in current clinical practice

Other Biologic Agents and Small Molecule Inhibitors in Giant Cell Arteritis

- Upadacitinib (JAK inhibitor) - *Blockmans et al. ARD 2024; 83 (suppl 1)*
  - Phase 3, RDBPC trial, 428 patients
  - 4 arms: UPA 7.5 mg/day, UPA 15 mg/day (both+Pred 26 weeks), Pred 26 weeks, Pred 52 weeks
  - Primary endpoint sustained remission Week 52: 46% UPA 15 mg vs 29% placebo (P=0.002)
    - UPA 7.5 mg/day did not meet the primary endpoint (41.1%)
  - No major adverse cardiovascular events occurred

Published Phase 2 trials – now in active Phase 3 trials

- Abatacept (CTLA4-Ig) - *Langford et al. A&R 2017;69:837*
  - 41 patients - Abatacept 10 mg/kg/month IV vs placebo (both + Prednisone 28-week taper)
  - 12-month relapse-free survival: 48% abatacept, 31% placebo (P=0.049)
  - Abatacept did not increase the frequency/severity of adverse events

- Secukinumab (anti-IL-17A) - *Venhoff et al. Lancet Rheumatol 2023;5:e341*
  - 52 patients - Secukinumab 300 mg SC/week vs placebo (both + Prednisolone 26-week taper)
  - Primary endpoint sustained remission 28 weeks: 70% secukinumab vs 20% placebo
  - Similar rate of adverse events

Recent Studies with Other Agents in Giant Cell Arteritis

- Mavrilimumab (anti-GM-CSF receptor) - *Cid et al. Ann Rheum Dis 2022;81:653*
  - 70 patients randomized 3:2 Mavrilimumab 150 mg SC q2 weeks vs placebo (both + Pred 26-week taper)
  - Primary endpoint: time to flare by Week 26: Mavrilimumab 19% vs placebo 46% (P=0.026)
  - Sustained remission Week 26: Mavrilimumab 83% vs placebo 50% (P=0.0038)
  - Adverse events similar between groups

- Ustekinumab (anti-IL-12/IL-23) – Mixed impressions
  - *Conway et al. ARD 2016;75:1578* – open label 14 patients – no relapses but 75% still on prednisone
  - *Matza et al. Arthritis Care Res 2021;73:893* – open label 13 patients – only 23% achieved primary endpoint

- Guselkumab (anti-IL-23) - Trial halted due to insufficient evidence of efficacy
- Sirukumab (anti-IL6) - *Schmidt et al. Rheumatol Ther 2020;7:793* - Trial halted by the sponsor
- Sarilumab (anti-IL6R) - *Schmidt et al. Arth Res Ther 2023;25:199* - Trial halted due to enrollment (COVID)

  - ➢ Positive study with sarilumab in PMR (*Spiera et al. N Engl J Med 2023;389:1263*)
    FDA approval 2/2023: PMR with inadequate response to GC or unable to tolerate GC taper

Treatment of Takayasu Arteritis

Glucocorticoids remain the foundation of treatment – limitations: relapse and intolerance

Investigating treatment options in Takayasu arteritis has been challenging

- Rare disease – difficult to have sufficient numbers for comparative trials
- Limitations of our current measures to assess disease activity
- Endpoints may not occur rapidly (particularly angiographic progression)

Almost all treatment data comes from retrospective series or small open-label studies

Conventional Immunosuppressive	**Number**	**Citation**
Methotrexate	16	*Hoffman et al. Arthritis Rheum 1994;37:578*
Azathioprine	15	*Valsakumar et al. J Rheum 2004;30:1793*
Mycophenolate mofetil	10 21	*Shinjo et al. Clin Rheum 2007;26:1871* *Goel et al. Clin Rheum 2010; 29:329*
Leflunomide	15 56	*de Souza et al. Sc J Rheum 2012;41:227* *Cui et al. Semin Arth Rheum* 2020;50:59

Experience with TNF inhibitors and Tocilizumab in Takayasu Arteritis

Numerous reports with the use of TNFi or tocilizumab (over 25 publications for each)

- TNF inhibitors
  - Studies dating back to 2004 – almost all retrospective
  - Most data with infliximab (dosing from 5 mg/kg every 8 weeks to 10 mg/kg every 4 weeks)

- Tocilizumab
  - Studies dating back to 2008 – almost all retrospective
  - Data with intravenous (IV) and subcutaneous (SC) (*Mekinian et al. RMD Open 2023;9*)
  - Prospective phase 4 observational study (*Harigai et al. Mod Rheumatol 2023;33:998*)
    - 120 patients treated with tocilizumab 162 mg/week SC
    - Relapse rate 20%
    - 83.0% of relapse-free patients reached prednisolone < 10 mg/day (25% = 0 mg)

Collective published findings suggest that TNFi and tocilizumab have efficacy in the ability to achieve and sustain remission and reduce glucocorticoids

Randomized Trial of Tocilizumab in Takayasu Arteritis

Nakaoka et al. ARD 2018;77:348, Nakaoka et al. Rheumatology 2020; 59:2427

- 36 patients with refractory TAK (relapse within past 12 weeks, were in remission ≥ 1 week)
  - Randomized to tocilizumab 162 mg/week or placebo
  - Background glucocorticoids were tapered by 10%/week to 0.1 mg/kg/day
  - Double blinding was halted when 19 of 36 patients relapsed
- Primary endpoint - time to first relapse
  - Intent to treat (18 TCZ vs 18 placebo): p=0.0596 – did not meet primary endpoint
  - Per protocol (16 TCZ vs 17 placebo): p=0.0345
- Long-term follow-up through week 96 suggested a glucocorticoid sparing effect
- No new safety concerns were identified

Tocilizumab did not influence time to relapse by intent to treat
By other analyses, there was a trend towards benefit

Comparisons of TNF inhibitors and Tocilizumab in Takayasu Arteritis

- *Wang et al. Rheumatology 2024;63:1359*
  - Open label randomized trial in 40 patients with active, severe TAK
    - 21 adalimumab, 19 tocilizumab, all received glucocorticoids (GC) and methotrexate
  - Efficacy rate at 6 months: 86% adalimumab vs 53% tocilizumab (p = 0.02)
  - Similar: ability to reach ≤ 10 mg GC at 6 months, relapse during 12 months, adverse event rate
- *Mekinian et al. Rheumatol 2022;61:1376*
  - Retrospective review of 209 patients – 132 TNFi (109 infliximab) and 77 tocilizumab
  - Complete response at 6 months: TNFi 66%, TCZ 70%
  - Incidence of relapse or treatment discontinuation was similar for TNFi and TCZ
- *Alibaz-Oner et al. Sem Arth Rheum 2021;51:1224*
  - Retrospective review of 111 patients (173 courses) – 119 TNFi (77 infliximab), 49 tocilizumab
  - Remission rates TNFi vs TCZ similar with similar ability to reduce/stop GC

Decisions about which agent to use should be based on individual factors

Other Biologic Agents and Small Molecule Inhibitors in Takayasu Arteritis

- Tofacitinib (JAK inhibitor)
  - *Kong et al. ARD 2022;81:117* - 53 patients - tofacitinib vs methotrexate (both + prednisone)
    - Tofacitinib statistically better: remission, relapse, median relapse-free duration, median pred dose
  - *Wang et al. Sem Ar Rheum 2022;55:152018* - 67 patients - tofacitinib vs leflunomide (both + prednisone)
    - Similar rate of effectiveness, relapse, higher toxicity with leflunomide

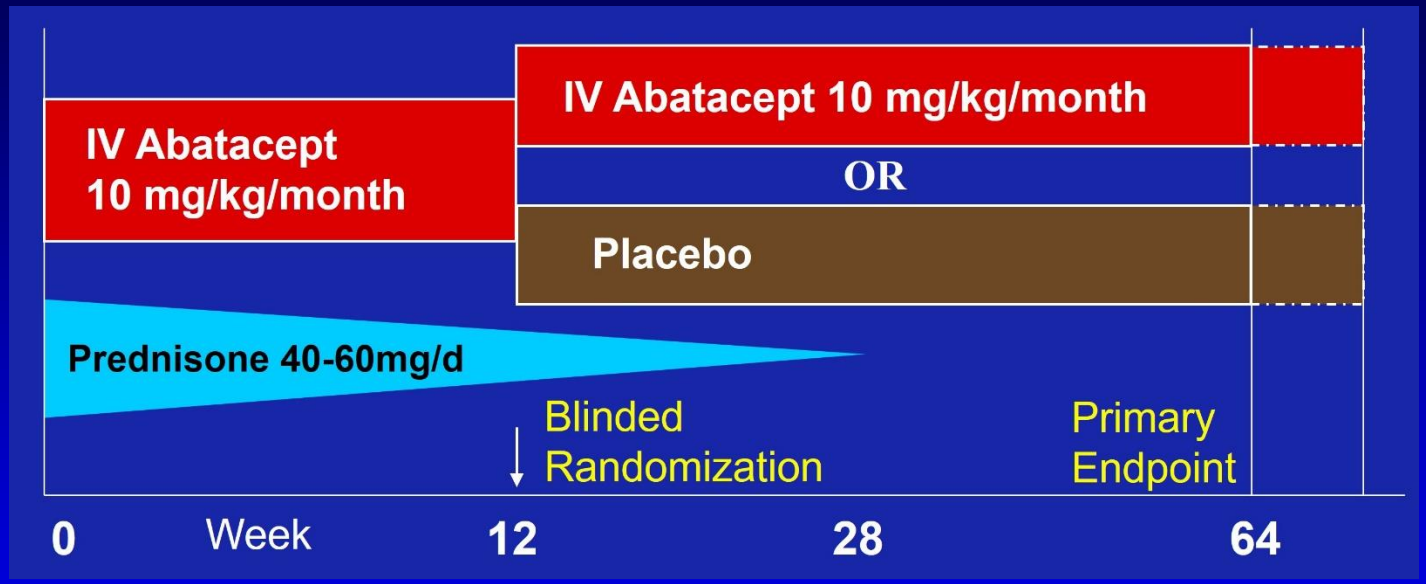
- Secukinumab (IL-17A monoclonal antibody) - *Tian et al. Arth Rheumatol 2023;75:1415*
  - 53 patients open-label study - secukinumab vs TNFi
  - Complete or partial response at 6 months: 53% secukinumab, 65% TNFi (p=0.389)

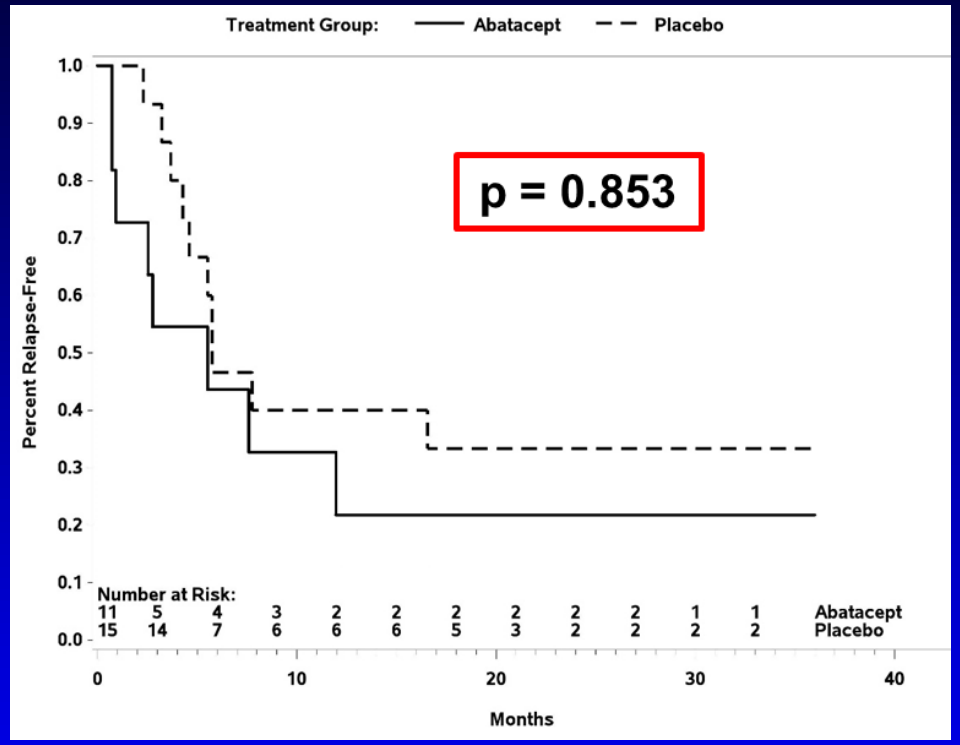
- Rituximab (anti CD20 monoclonal antibody) - *Mekinian et al. Joint Bone Spine 2024;91:105658*
  - 11 patients retrospective report and literature review of 28 patients
  - Minimal evidence to support efficacy

Insufficient evidence to support current use of any these agents in clinical practice
Tofacitinib and Secukinumab may warrant further investigation

Abatacept (CTLA4-Ig) in Takayasu Arteritis

Langford et al. A&R 2017;69:846





- Results
  - 34 patients treated, 26 randomized (11 abatacept, 15 placebo)
  - 12-month relapse-free survival: 22% abatacept vs 40% placebo (P=0.853)
  - Abatacept did not increase the frequency/severity of adverse events

Abatacept did not reduce the risk of relapse in Takayasu arteritis

Comparing and Contrasting the Treatment Experience in Giant Cell Arteritis and Takayasu Arteritis

	Giant cell arteritis	Takayasu arteritis
Glucocorticoids	+++	+++
Methotrexate	++	+
Azathioprine	+	+
TNF inhibitors	-	++
Tocilizumab	+++	++
Abatacept	++	-

Randomized trials

Retrospective or open-label studies

Treatment experience suggests some differences in response between giant cell arteritis and Takayasu arteritis

Giant Cell Arteritis and Takayasu Arteritis

Non-Medical Management of Large Vessel Disease

Surgical treatment for sequelae of aneurysmal disease

- aortic root / valve replacement
- aortic aneurysm thoracic / abdominal

Non-medical management of fixed stenotic lesions causing ischemia

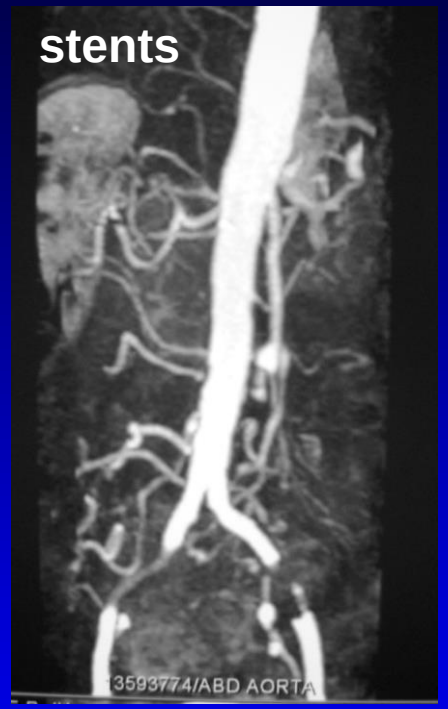
- Severe limb claudication affecting quality of life
- CNS: TIA / cerebral ischemia / stroke
- Renal artery stenosis (hypertension, renal insufficiency)
- Angina
- Bowel ischemia / infarction

Interventional recommendations:

- If possible, avoid intervention during active disease
- Base stenosis intervention on symptoms – not just presence of lesion
- Avoid arm intervention unless symptoms are severe – collateral potential

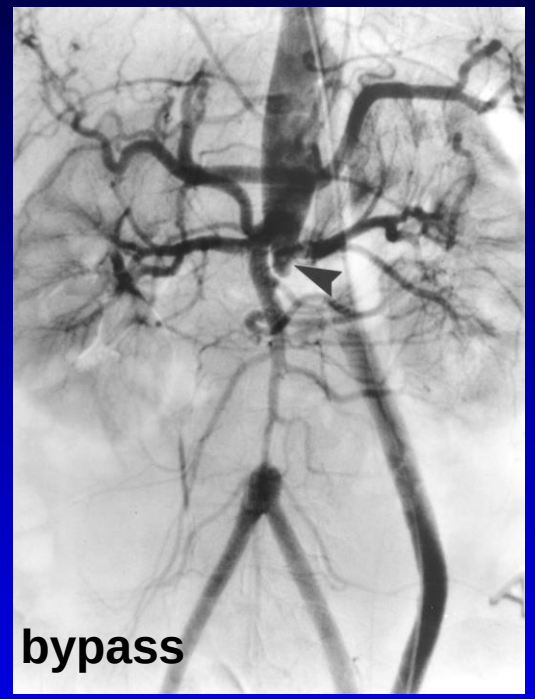
Giant Cell Arteritis and Takayasu Arteritis

Non-Medical Management of Large Vessel Disease



Modalities:

- PCTA
- Stent
- Open surgical bypass



Liang et al. J Rheumatol 2004; 31:102

- Endovascular revascularization procedures (PCTA, stent)
  - favorable safety with low morbidity/mortality
  - high long-term failure rate in TAK
- Surgical bypass grafts had the best long-term outcome

Conclusion: Giant Cell Arteritis and Takayasu Arteritis

Recent years have seen significant advances in our understanding of the role of imaging and novel treatment approaches in these diseases

Key areas of ongoing challenges:

- Relapse
- Treatment toxicity
- Patient quality of life

Opportunities and questions:

- Understanding disease mechanisms will continue to provide opportunities for intervention
- Should cranial and large vessel disease in GCA be treated similarly ?
- Does controlling disease symptoms mean control of vascular inflammation ?
  - If not, does this matter if the patient is clinically doing well ?
- How do we assess disease activity and treatment response in GCA and TAK ?