

# Vasculitis Roundup 2017



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# Objectives

1. Update on Small, Medium and Large Vessel Vasculitis
2. Update on Imaging in Vasculitis
3. Update on Treatment in a variety of vasculitides

# The 18th International Vasculitis & ANCA Workshop

—Diversity and Integration for Tomorrow—

25(Sat.)- 28(Tue.) March 2017

Ito International Research Center, The University of Tokyo, Tokyo, Japan







# The 18th International Vasculitis & ANCA Workshop in Tokyo

- Diversity and Integration for Tomorrow

Saturday, March 25  
- Tuesday, March 28, 2019

Oral Sessions:  
Ito International Research Center,  
The University of Tokyo

Poster Sessions:  
Masuda Auditorium

President: Yoshihiro Arimura  
Kyorin University school of Medicine





# Large Vessel Vasculitis



# CASE

33 yo woman with Takayasu's arteritis diagnosed August 2011 with infrarenal aorta stenosis, proximal left common iliac, right common iliac, celiac artery, complete occlusion of SMA, R renal artery, stenosis of L accessory renal artery, R pulmonary artery system.

HTN

R kidney atrophy

Currently asymptomatic. CRP 10.3

## Current Medications

PREDNISONE 5 MG TABS (PREDNISONE) 5 mg po daily

FOSAVANCE 70-5600 MG-UNIT TABS 1 tab po qweekly

NORVASC 10 MG TABS (AMLODIPINE BESYLATE) 10mg po daily

AMILORIDE HCL 5 MG TABS (AMILORIDE HCL) 5mg po daily

LABETALOL HCL 100 MG TABS (LABETALOL HCL) 1 tab po bid

IRBESARTAN 300MG PO DAILY

Physical exam BP 132/80 R and 138/80 L

Brachial and radial pulses normal. No subclavian or carotid bruits.

Abdominal bruit, bilateral renal bruit, L iliac bruit

Is she in remission? How to assess disease activity?

# CASE

What imaging would you perform next as followup to assess disease activity?

1. Doppler ultrasound of abdominal vessels
2. CT Angiogram
3. MR Angiogram
4. PET/CT Scan
5. PET/MRI Scan

# IMAGING IN TAKAYASU'S





## **PI\_7 Discrepancies Between Clinical- and Imaging-Based Assessments of Disease Activity in Takayasu's Arteritis**

**Objectives:** To study the relationship between clinically-determined disease activity and vascular inflammation assessed by positron emission tomography (PET) in patients with Takayasu's arteritis (TAK).

**Methods:** Patients with new or relapsing TAK were evaluated at 5 centers.

Whole body  $^{18}\text{F}$ -FDG-PET CT imaging was performed during a period of clinical disease activity.

Clinical assessments were performed blinded to PET scan findings.

A single nuclear medicine physician interpreted all of the PET scans, blinded to clinical data, to determine presence of active vasculitis based on degree of arterial FDG uptake.

Classification and regression tree analysis (CART) defined predictors of PET scan activity.

## **PI\_7 Discrepancies Between Clinical- and Imaging-Based Assessments of Disease Activity in Takayasu's Arteritis**

**Methods:** Elevated acute phase reactants (ESR > 30mm/hr, CRP > 10mg/L), prednisone dose at time of imaging, ongoing use of other immunosuppressive agents for > 1 month at time of clinical assessment, and clinical features of disease activity (vascular vs nonspecific) were studied.

Non-specific features of disease activity were defined as constitutional symptoms accompanied by elevated acute phase reactants in the absence of signs or symptoms of vascular involvement.

## PI\_7 Discrepancies Between Clinical- and Imaging-Based Assessments of Disease Activity in Takayasu's Arteritis

**Results:** Clinical assessments were performed in 25 patients with TAK, and PET scans were performed a median of 7 days later.

FDG-PET findings were suggestive of active vasculitis in 13 of 25 patients (52%).

Interval increase in glucocorticoid therapy between clinical assessment and imaging occurred in 6/13 (46%) patients with an active scan and 9/12 (75%) patients with an inactive scan ( $p = 0.23$ ).

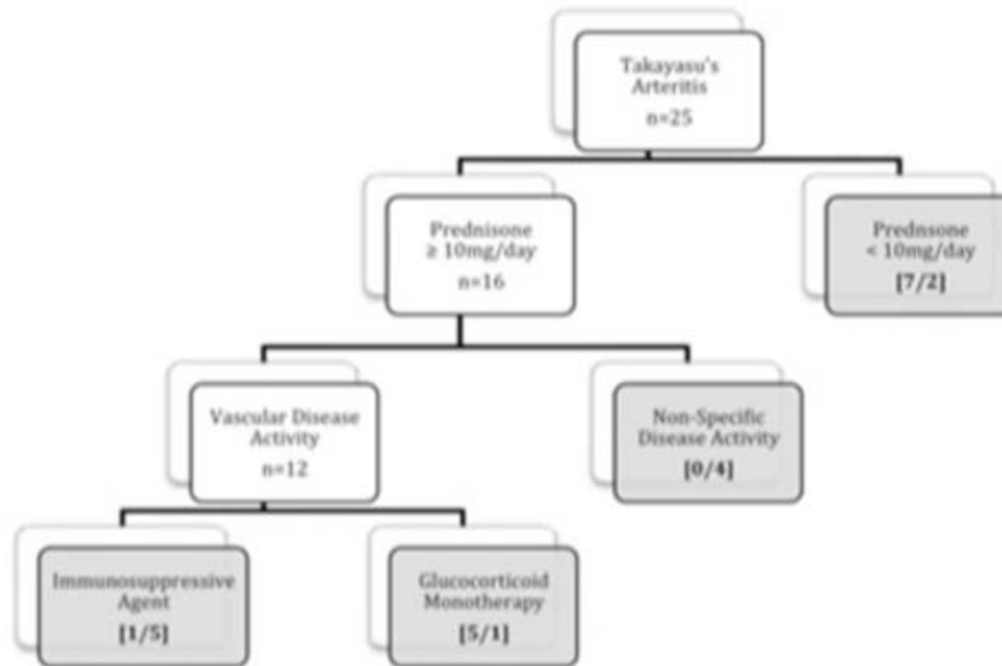
CART analysis predicted FDG-PET scan activity with 84% accuracy based upon 3 variables: prednisone dose at the time of imaging, clinical features of disease activity, and use of a non-glucocorticoid immunosuppressive agent

Acute phase reactants were not predictive within the model.

Prednisone use was the strongest determinant of vascular activity on FDG-PET. Among patients on high doses of prednisone, clinical features of vascular symptoms and treatment with glucocorticoid monotherapy were associated with increased probability of active vasculitis on imaging.



## PI\_7 Discrepancies Between Clinical- and Imaging-Based Assessments of Disease Activity in Takayasu's Arteritis



**Figure. Classification and regression tree analysis (CART) to Determine Predictors of PET Scan Activity in Takayasu's Arteritis.** Amount of daily prednisone, nature of disease activity, and ongoing use of a non-glucocorticoid immunosuppressive agent at the time of initial clinical assessment were predictors of PET scan activity in the cohort. Brackets within terminal nodes (grey boxes) depict the number of patients with [abnormal PET scan / normal PET scan]. CART model predicted PET scan activity with an accuracy of 84% (21 out of 25 patients classified correctly).

## **PI\_7 Discrepancies Between Clinical- and Imaging-Based Assessments of Disease Activity in Takayasu's Arteritis**

**Conclusions:** Clinical features of disease and treatment status are associated with different findings on vascular FDG-PET scan in TAK.

Imaging-based assessment of disease activity provides unique and complimentary information compared to clinical assessment in TAK and may enable patient stratification strategies for future clinical trials.

# Treatment in Takayasu's





# CASE

25 yo with Takayasu's since 2007 stenting surgery Feb 2010 of thoracoabdominal coarctation aorta. Bilateral carotid and renal bruits, decreased left radial and brachial pulses, tiredness and fatigue, low back pain, and peak elevation of ESR to 40 and CRP of 53)  
-Involvement of right common carotid, left axillary, abdominal aorta, right renal and subsegmental pulmonary arteries

## **Past Medications**

Methotrexate and Remicade from November 2008-February 2010.

She had pancreatitis with Imuran.

She was switched from Feb 2010 to Humira and Methotrexate and Arava.

Humira was stopped July 2010 because of difficulty in injecting with it.

Arava was also stopped July 2010 because of diarrhea.

Restarted on Remicade in July 2010 and was on MTX concomitantly.

Increasing claudication and MRI new R axillary stenoses, moderate progressive left renal stenosis and new severe SMA stenosis

What should next agent be?

## A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Takayasu Arteritis

Carol A. Langford,<sup>1</sup> David Cuthbertson,<sup>2</sup> Steven R. Ytterberg,<sup>3</sup> Nader Khalidi,<sup>4</sup>  
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for the Vasculitis Clinical Research Consortium

# NIH Criteria for active disease in TAK

## **Criteria for Active Disease in Patients with Takayasu Arteritis\***

1. Systemic features, such as fever, musculoskeletal (no other cause identified)
2. Elevated erythrocyte sedimentation rate
3. Features of vascular ischemia or inflammation, such as claudication, diminished or absent pulse, bruit, vascular pain (carotodynia),
4. asymmetric blood pressure in either upper or lower limbs (or both)
5. Typical angiographic features

\* New onset or worsening of two or more features indicates "active disease."



# **A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Takayasu Arteritis**

**Objective:** To compare the efficacy of abatacept to that of placebo for the treatment of Takayasu arteritis (TAK).

**Methods:** Patients with newly-diagnosed or relapsing TAK were eligible for the trial.

All patients were treated with abatacept 10 mg/kg IV on days 1, 15, 29, and week 8, together with prednisone.

At week 12 patients in remission underwent a double-blinded randomization to continue monthly abatacept or be switched to placebo together with a standardized prednisone taper reaching discontinuation at week 28.

Patients remained on their randomized assignment until meeting criteria for early termination or until the common closeout date, 12 months after enrollment of the last patient.

The primary endpoint was duration of remission (relapse-free survival, RFS).

## **A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Takayasu Arteritis**

**Results:** 34 eligible patients received study drug with 26 reaching the week 12 randomization.

There was no statistical difference in the baseline or disease characteristics of the randomized patients.

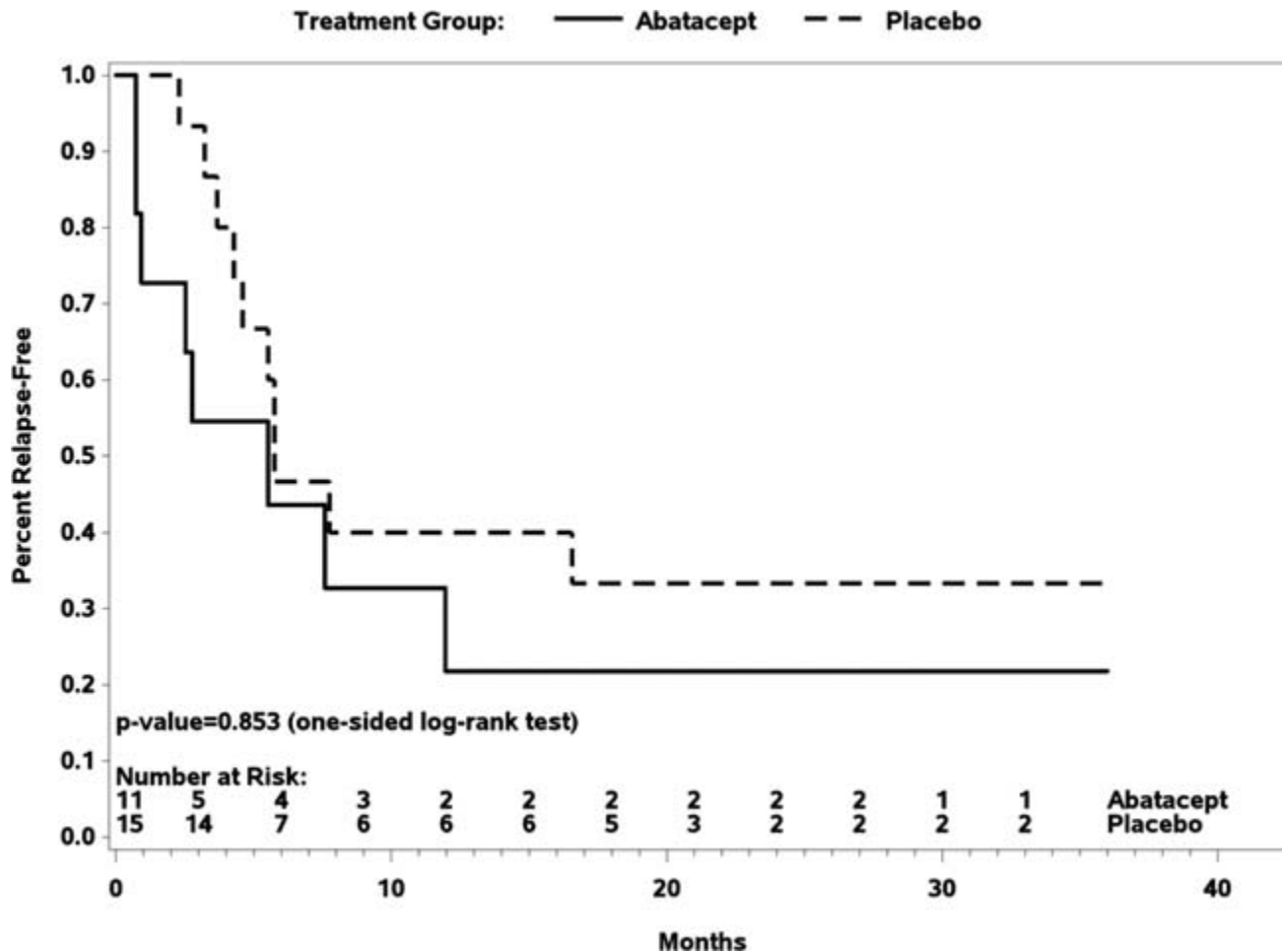
The RFS at 12 months was estimated to be 22% for those receiving abatacept and 40% for those receiving placebo ( $p = 0.853$ )

Treatment with abatacept in patients with TAK enrolled in this study was not associated with a longer median duration of remission (abatacept 5.5 months, placebo 5.7 months).

114 adverse events occurred in 28 patients including 24 serious adverse events in 15 patients.

There was no difference in the frequency or severity of adverse events between treatment arms, including the rate of infection.

# A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Takayasu Arteritis



## **A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Takayasu Arteritis**

**Conclusions:** In this study, which was the first randomized, double-blind trial conducted in TAK, the addition of abatacept to prednisone did not reduce the risk of relapse in patients with TAK.

Concurrent abatacept was not associated with a higher rate of toxicity compared to prednisone alone.

# CASE

She received Abatacept from August 4, 2011 to October 21, and flared with discontinuation from infusions January 6, 2012.

Restarted Remicade and Methotrexate February 2012 to February 2014

May 2014 increasing claudication symptoms.

Now what?



## **WS5\_2 Efficacy and Safety of Subcutaneous Tocilizumab in Japanese Patients with Refractory Takayasu Arteritis: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial**

**Objectives:** To investigate the efficacy and safety of the interleukin-6 receptor antibody, tocilizumab in patients with Takayasu arteritis (TAK).

**Methods:** Patients with TAK who relapsed within 12 weeks of enrolment despite receiving treatment with oral glucocorticoid (GC) at a prednisolone-equivalent dose of at least 0.2 mg/kg/day were enrolled.

Patients were randomly assigned 1:1 to receive weekly tocilizumab 162 mg or placebo subcutaneously after achieving remission with oral GC therapy at least twice that of the relapse dose.

During the double-blind period (until 19 patients relapsed), GCs were tapered 10%/week from week 4.

The primary endpoint was time-to-relapse of TAK defined as  $\geq 2$  of: objective systemic symptoms; subjective systemic symptoms; elevated inflammation markers; vascular lesions; or ischemic symptoms accompanied by organ lesions in the intent-to-treat (ITT) population.

## **WS5\_2 Efficacy and Safety of Subcutaneous Tocilizumab in Japanese Patients with Refractory Takayasu Arteritis: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial**

**Results:** The ITT and safety populations included 18 tocilizumab-treated and 18 placebo-treated patients.

The per-protocol set (PPS) included 16 tocilizumab-treated and 17 placebo-treated patients.

The mean  $\pm$  SD dose of prednisolone-equivalent GC at baseline was  $32.1 \pm 18.7$  mg/day in tocilizumab group and  $29.7 \pm 6.8$  mg/day in placebo group.

Hazard ratio for time-to-relapse of TAK were

0.41 (95.41%CI: 0.15, 1.10; log-rank P = 0.0596) in the ITT population (based on relapse in 8 tocilizumab-treated and 11 placebo-treated patients)

0.34 (95.41%CI: 0.11, 1.00; log-rank P = 0.0345) in the PPS (7 tocilizumab-treated and 11 placebo-treated patients, respectively)

## **WS5\_2 Efficacy and Safety of Subcutaneous Tocilizumab in Japanese Patients with Refractory Takayasu Arteritis: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial**

**Results:** The secondary endpoints, time to relapse assessed by Kerr's definition or clinical symptoms only, showed a consistent trend favouring tocilizumab.

The oral prednisolone-equivalent GC dose was reduced to 10 mg/day or less at last observation of double-blind period in 11 (61%) tocilizumab-treated and 7 (39%) placebo-treated patients.

Infections were reported in 9 (50%) tocilizumab-treated and 6 (33%) placebo-treated patients; serious adverse events were reported in 1 and 2 patients, respectively.

There were no serious infections and deaths.

## **WS5\_2 Efficacy and Safety of Subcutaneous Tocilizumab in Japanese Patients with Refractory Takayasu Arteritis: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial**

### **Conclusions:**

Although the primary endpoint was not met, a trend favoured tocilizumab over placebo for time-to-relapse of TAK and safety was consistent with the known safety profile of tocilizumab.

# CASE

Actemra 8mg/kg May 2014 until July 2015

July 2015 increasing claudication symptoms.

Now what?



## PI\_26 Efficacy of Rituximab in Takayasu Arteritis:A Case Series

**Objectives:** This study aimed to investigate the efficacy of rituximab (RTX) in patients with Takayasu arteritis (TAK).

**Methods:** Nine patients were identified by retrospective chart review from local registries at three University Hospitals in Europe.

All patients met Chapel Hill 2012 Consensus Conference definitions of TAK.

Assessed the dose of steroid treatment, C-reactive protein (CRP) and NIH criteria by Kerr before and after RTX administration.

## PI\_26 Efficacy of Rituximab in Takayasu Arteritis: A Case Series

**Results:** One patient was excluded because essential data were lacking.

6 female and 2 male were evaluated.

Median age was 38 years, while disease duration until RTX administration was 5 years.

RTX was the first biologic agent used in 5 patients.

Daily dose of steroids significantly decreased between baseline and after 48 weeks of follow-up ( $P = 0.012$ ).

In line with steroid reduction, NIH criteria for disease activity assessment decreased between baseline and 48 weeks ( $P = 0.016$ ).

There was no difference in CRP ( $p = 0.914$ ). No relapse after RTX administration was observed during the follow-up period of 48 weeks.

Among side effects, one patient developed a severe allergic reaction after the second infusion of rituximab.

## PI\_26 Efficacy of Rituximab in Takayasu Arteritis:A Case Series

**Conclusions:** This case series highlight efficacy of RTX in patients with difficult to treat TAK.

More studies in this context in a prospective manner are necessary to establish B-cell depletion with RTX as a treatment option of TAK.

# CASE

Rituximab q6monthly given since February 2016 with no symptoms and followup imaging no new areas of stenoses.

# GIANT CELL ARTERITIS: Biopsy





## **WS5\_3 Differences in Presentation and Outcome in Patients with Giant Cell Arteritis Based on Temporal Artery Biopsy Positivity**

**Objectives:** To establish a large-single institution cohort of patients with temporal artery biopsy-negative giant cell arteritis (GCA). To identify differences in presentation and outcome among patients with biopsy-negative and biopsy-positive GCA.

**Methods:** Patients with temporal artery biopsy-negative GCA diagnosed between 1/1/1998 and 12/31/2013 were identified retrospectively.

Final diagnosis was confirmed by consensus among two rheumatologists and a physician abstractor.

Baseline characteristics and outcomes were compared to a previously established biopsy-positive GCA cohort (n=286) from the same institution.

## **WS5\_3 Differences in Presentation and Outcome in Patients with Giant Cell Arteritis Based on Temporal Artery Biopsy Positivity**

**Results:** 98 patients with temporal artery biopsy-negative GCA were identified.

Unilateral biopsies were performed in 65, bilateral-sequential in 9, and bilateral same day in 24 cases.

Median duration between steroid initiation and biopsy was 4 days.

Median length of first biopsy was 13.5mm and second biopsy (if performed) was 23mm.

Among patients with advanced imaging within 6-months of diagnosis, 62% (33/53) had evidence of large vessel vasculitis.

Patients with biopsy-negative GCA were younger ( $72.4 \pm 9.0$  vs  $75.0 \pm 7.6$ ;  $p=0.006$ ), met fewer ACR criteria ( $\geq 3$  criteria 67% vs 95%;  $p<0.001$ ) and had a shorter time from symptom onset to diagnosis (median 1.1 vs 2.1 months;  $p<0.001$ ).

Headache and vision loss were similar between groups.

## **WS5\_3 Differences in Presentation and Outcome in Patients with Giant Cell Arteritis Based on Temporal Artery Biopsy Positivity**

**Results:** Biopsy-negative GCA patients had more temporal artery tenderness (37% vs 16%;  $p<0.001$ ) and transient visual symptoms (34% vs 23%;  $p=0.036$ ) but less frequent jaw claudication (22% vs 52%;  $p<0.001$ ).

Anorexia, fatigue, and arthralgia were more frequent in biopsy-negative patients.

Baseline CRP was lower among patients with negative biopsies ( $44.8\pm54.7$  vs  $70.4\pm63.9$  mg/L;  $p<0.001$ ).

Initial prednisone dose was similar among both cohorts. Although cumulative glucocorticoid (GC) was lower in biopsy-negative patients at 1 year ( $6.0\pm2.3$  vs  $7.2\pm2.7$  g;  $p<0.001$ ), cumulative GC doses at 2-years and 5-years were equivalent.

Biopsy-positive patients (5-years,  $56\pm3\%$ ) were able to discontinue GC sooner than biopsy-negative patients (5-years,  $28\pm5\%$ ;  $p=<0.001$ ).

The number of relapses, time-to-first relapse and annual relapse rate did not differ based on biopsy positivity.

## **WS5\_3 Differences in Presentation and Outcome in Patients with Giant Cell Arteritis Based on Temporal Artery Biopsy Positivity**

**Conclusions:** While similarities are present, notable differences are observed at diagnosis in patients with biopsy-negative GCA.

# GIANT CELL ARTERITIS: Imaging





## PI\_45 Arterial Lesions in Giant Cell Arteritis

**Objectives:** Descriptive study of large arterial lesions among patients with giant cell arteritis (GCA) and evaluated clinical characteristics associated with development of new arterial lesions.

**Methods:** Patients with GCA enrolled in a prospective, multicenter, longitudinal study and/or a clinical trial (AGATA) were included.

All patients were followed with standardized clinical assessments, including data from arterial imaging (stenoses, occlusions, aneurysms, and dissections).

New lesions were defined as new findings in a previously unaffected arterial segment.

## PI\_45 Arterial Lesions in Giant Cell Arteritis

**Results:** Data on imaging of the aorta and its branches were available for 187 patients: 146 (78%) female, mean ( $\pm$  SD) age at diagnosis 68.5 ( $\pm$  8.5) years.

Mean ( $\pm$  SD) duration of follow-up from entry into the cohort was 3.8 ( $\pm$  2.3) years.

At least one arterial lesion was present in 123 (66%) patients on entry into the cohort

Serial imaging was available in 106 (57%)

New arterial lesions were noted in 41 (39%).

## PI\_45 Arterial Lesions in Giant Cell Arteritis

**Results:** Clinical symptoms of any active disease since the last visit were present in 20/73 visits (28%) with a new angiographic lesion.

All patients with new lesions had at least 1 arterial lesion at first imaging.

There were no differences in age, sex, disease duration, duration of follow-up, or presence of any disease activity during follow-up

## PI\_45 Arterial Lesions in Giant Cell Arteritis

**Conclusions:** Subclavian and axillary artery involvement were the most frequently observed large-vessel lesions in patients with GCA at first imaging and during follow-up.

All new lesions in this study occurred among patients with established large-vessel involvement.

New lesions identified on serial angiography occurred in patients without symptoms of active disease.

These data expand our understanding of large-arterial disease in GCA, support the need to conduct serial imaging in GCA, and will inform design of clinical trials in GCA.

# GIANT CELL ARTERITIS: Treatment



BEFORE 2017

# GIANT CELL ARTERITIS: Treatment



**AFTER 2017 (we hope!)**

## A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Giant Cell Arteritis

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# **A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Giant Cell Arteritis**

**Objective:** To compare the efficacy of abatacept to that of placebo for the treatment of GCA.

**Methods:** Patients with newly-diagnosed or relapsing TAK were eligible for the trial.

All patients were treated with abatacept 10 mg/kg IV on days 1, 15, 29, and week 8, together with prednisone.

At week 12 patients in remission underwent a double-blinded randomization to continue monthly abatacept or be switched to placebo together with a standardized prednisone taper reaching discontinuation at week 28.

Patients remained on their randomized assignment until meeting criteria for early termination or until the common closeout date, 12 months after enrollment of the last patient.

The primary endpoint was duration of remission (relapse-free survival, RFS).

## **A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Giant Cell Arteritis**

**Results:** Forty-nine eligible patients with GCA were enrolled and treated with prednisone and abatacept; of these, 41 reached the week 12 randomization and underwent a blinded randomization to receive abatacept or placebo.

Prednisone was tapered using a standardized schedule, reaching a daily dosage of 20 mg at week 12 with discontinuation in all patients at week 28.

The relapse-free survival rate at 12 months was 48% for those receiving abatacept and 31% for those receiving placebo ( $P = 0.49$ ).

A longer median duration of remission was seen in those receiving abatacept compared to those receiving placebo (median duration 9.9 months versus 3.9 months;  $P = 0.23$ ).

There was no difference in the frequency or severity of adverse events, including infection, between the treatment arms.

## **A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Giant Cell Arteritis**

**Conclusion:** In patients with GCA, the addition of abatacept to a treatment regimen with prednisone reduced the risk of relapse and was not associated with a higher rate of toxicity compared to prednisone alone.

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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

# Trial of Tocilizumab in Giant-Cell Arteritis (GiACTA)

## **BACKGROUND**

Giant-cell arteritis commonly relapses when glucocorticoids are tapered, and the prolonged use of glucocorticoids is associated with side effects.

The effect of the interleukin-6 receptor alpha inhibitor tocilizumab on the rates of relapse during glucocorticoid tapering was studied in patients with giant-cell arteritis.

# Trial of Tocilizumab in Giant-Cell Arteritis (GiACTA)

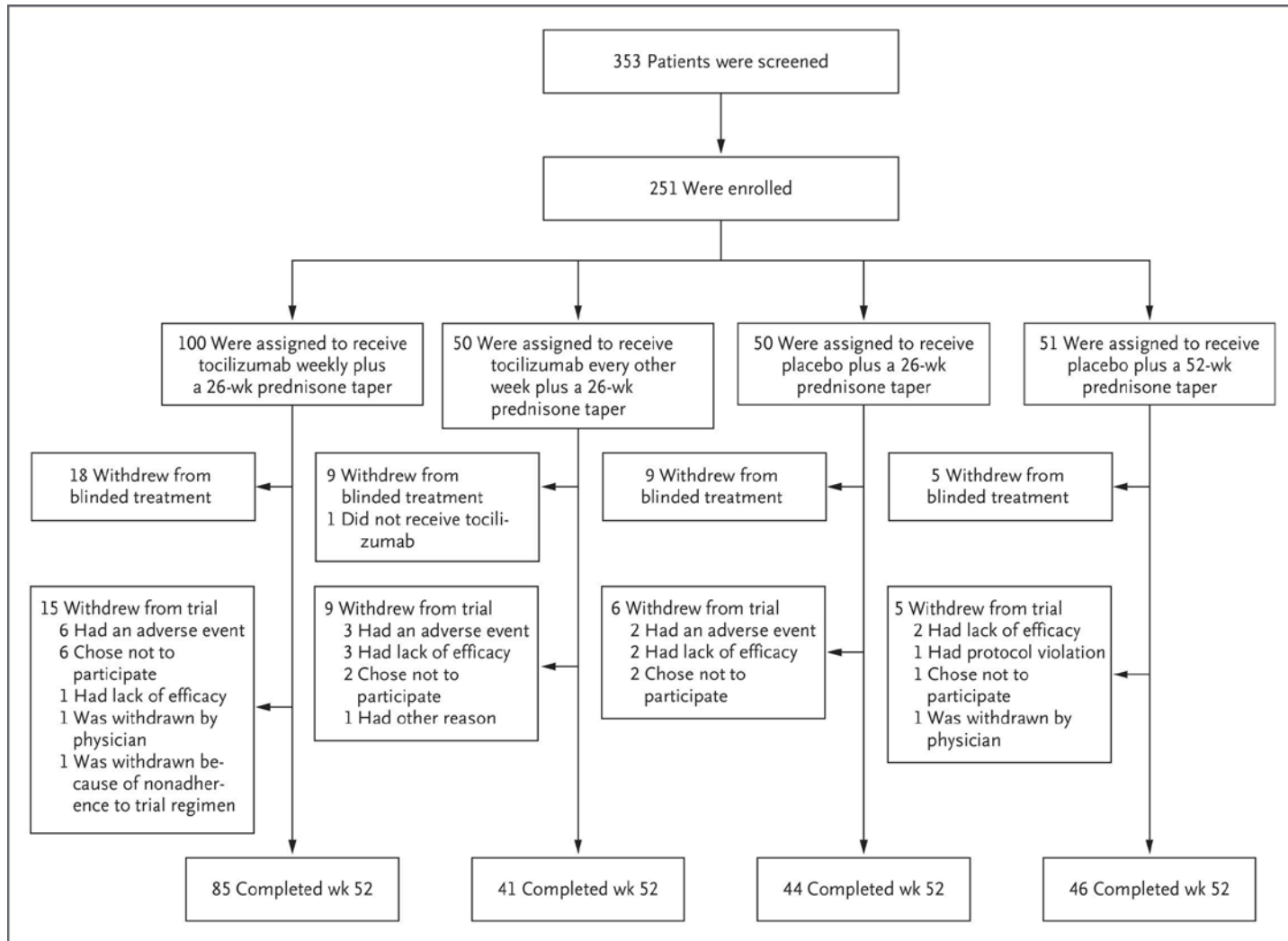
## **METHODS**

In this 1-year trial, 251 patients were randomly assigned in a 2:1:1:1 ratio, to receive subcutaneous tocilizumab (at a dose of 162 mg) weekly or every other week, combined with a 26-week prednisone taper, or placebo combined with a prednisone taper over a period of either 26 weeks or 52 weeks.

The primary outcome was the rate of sustained glucocorticoid-free remission at week 52 in each tocilizumab group as compared with the rate in the placebo group that underwent the 26-week prednisone taper.

The key secondary outcome was the rate of remission in each tocilizumab group as compared with the placebo group that underwent the 52-week prednisone taper.

Dosing of prednisone and safety were also assessed.





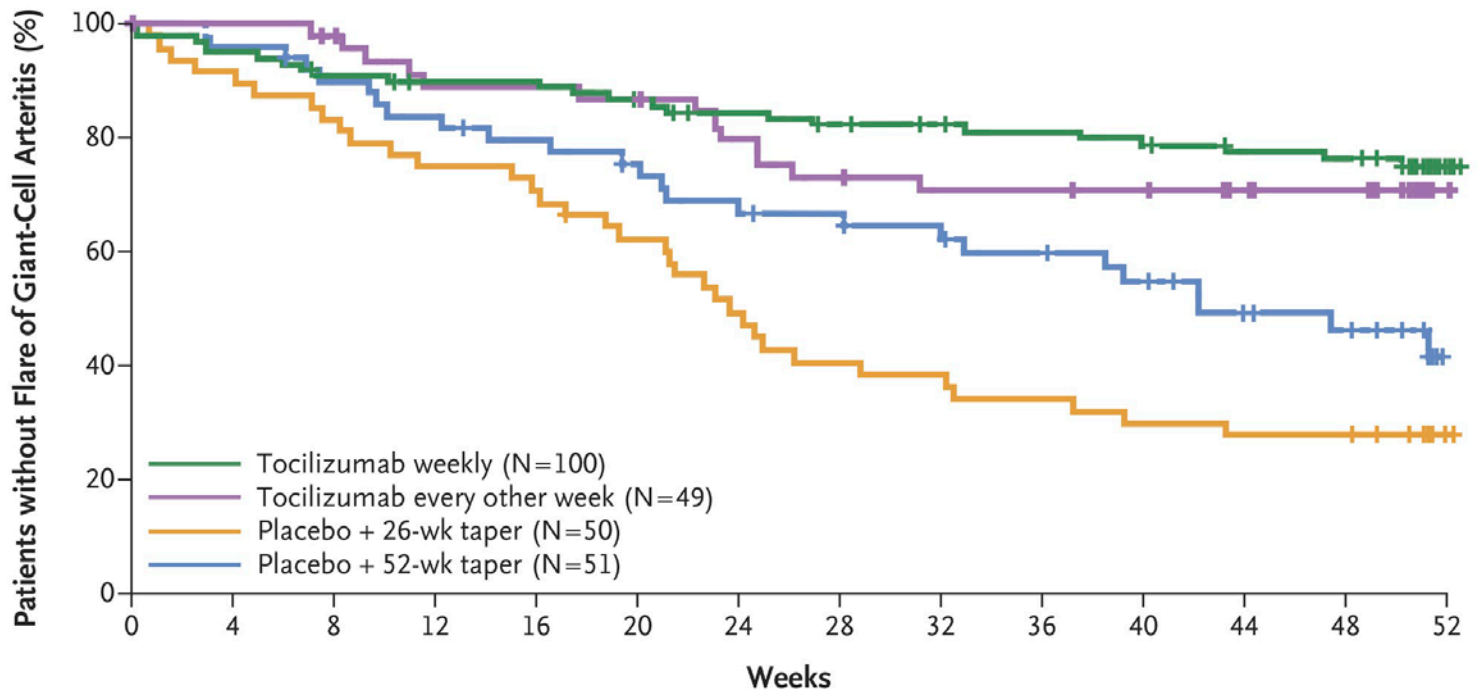
# Trial of Tocilizumab in Giant-Cell Arteritis (GiACTA)

## RESULTS

Sustained remission at week 52 occurred in  
56% of the patients treated with tocilizumab weekly  
53% of those treated with tocilizumab every other week,  
14% of those in the placebo group that underwent the 26-week prednisone taper  
18% of those in the placebo group that underwent the 52-week prednisone taper ( $P < 0.001$  for the comparisons of either active treatment with placebo).

The cumulative median prednisone dose over the 52-week period was  
1862 mg in each tocilizumab group  
3296 mg in the placebo group that underwent the 26-week taper ( $P < 0.001$  for both comparisons) 3818 mg  
in the placebo group that underwent the 52-week taper ( $P < 0.001$  for both comparisons).

Serious adverse events occurred in  
15% of the patients in the group that received tocilizumab weekly  
14% of those in the group that received tocilizumab every other week  
22% of those in the placebo group that underwent the 26-week taper  
25% of those in the placebo group that underwent the 52-week taper.



**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

**Table 2. Efficacy at Week 52 in the Intention-to-Treat Population.\***

Outcome	Tocilizumab Weekly (N = 100)	Tocilizumab Every Other Week (N = 49)	Placebo + 26-Wk Taper (N = 50)	Placebo + 52-Wk Taper (N = 51)
<b>Sustained remission with adherence to protocol-defined prednisone dose at wk 52</b>				
Patients with sustained remission at wk 52 — no. (%)	56 (56)	26 (53)	7 (14)	9 (18)
Primary outcome: unadjusted difference in rate of sustained remission vs. placebo + 26-wk taper (99.5% CI) — percentage points†	42 (18 to 66)	39 (12 to 66)	—	—
P value	<0.001	<0.001		
Key secondary outcome: unadjusted difference in rate of sustained remission vs. placebo + 52-wk taper (99.5% CI) — percentage points†	38 (18 to 59)	35 (10 to 60)	—	—
P value	<0.001	<0.001		
<b>Sustained remission, excluding normalization of CRP concentration, with adherence to protocol-defined prednisone dose at wk 52</b>				
Patients with sustained remission at wk 52, excluding normalization of CRP concentration — no. (%)	59 (59)	27 (55)	10 (20)	17 (33)
<b>Sensitivity analyses</b>				
For primary outcome of unadjusted difference in rate of sustained remission vs. placebo + 26-wk taper (99.5% CI) — percentage points†	39 (15 to 63)	35 (8 to 62)	—	—
P value	<0.001	<0.001		
For key secondary outcome of unadjusted difference in rate of sustained remission vs. placebo + 52-wk taper (99.5% CI) — percentage points†	26 (3 to 49)	22 (–6 to 49)	—	—
P value	0.003	0.03		
<b>Cumulative prednisone dose</b>				
<b>Expected cumulative dose — mg‡</b>				
Median	1337	1442	1337	2608
Range	350 to 2632	332 to 2632	952 to 2632	822 to 3902
<b>Actual cumulative dose — mg§</b>				
Median	1862	1862	3296	3818
Range	630 to 6602	295 to 9912	932 to 9778	822 to 10,698
P value vs. each placebo group	<0.001	<0.001		

\* Values are for the patients who had sustained remission while adhering to the protocol-defined prednisone dose at week 52, except as noted. Patients who had a flare, received escape therapy, withdrew from the trial, did not adhere to the protocol-defined prednisone taper, did not have remission by week 12, or had an elevated concentration of C-reactive protein (CRP) followed by an elevated or missing CRP concentration at the next assessment (except for the sensitivity analyses, from which these patients were excluded) were classified as not having had a response with respect to sustained remission.

† P values were calculated by a Cochran–Mantel–Haenszel test for superiority, with adjustment for the baseline prednisone dose ( $\leq 30$  mg per day vs.  $> 30$  mg per day).

‡ The values for the expected cumulative dose were based on a patient's starting prednisone dose in the taper, assuming that the taper was continued without error.

§ The values for the actual cumulative dose were based on actual records of prednisone taken and included all escape therapy and use of commercial prednisone as well as the prednisone used in the tapering process. P values were calculated by a van Elteren test that was stratified according to the baseline prednisone dose ( $\leq 30$  mg per day vs.  $> 30$  mg per day). For any records of missed tablets from the protocol-defined taper of prednisone, the missed tablets were assumed to be the minimum-dose tablets available from that pack. Patients who received an increased dose of prednisone because they entered escape therapy were included in their originally assigned treatment group. No imputation of missing data was implemented.



**Table 3. Safety over the 52-Week Trial Period.\***

Variable	Tocilizumab Weekly (N = 100)	Tocilizumab Every Other Week (N = 49)	Placebo + 26-Wk Taper (N = 50)	Placebo + 52-Wk Taper (N = 51)
Duration in trial — patient-yr	92.9	45.6	47.4	48.1
Patients with $\geq 1$ adverse event — no. (%)	98 (98)	47 (96)	48 (96)	47 (92)
Adverse events				
No. of events	810	432	470	486
Rate per 100 patient-yr (95% CI)	872.0 (813.0–934.2)	948.0 (860.7–1041.7)	990.8 (903.2–1084.5)	1011.2 (923.3–1105.3)
Patients with $\geq 1$ infection — no. (%)				
Any	75 (75)	36 (73)	38 (76)	33 (65)
Serious	7 (7)	2 (4)	2 (4)	6 (12)
Patients who withdrew from the trial because of adverse events — no. (%)†	6 (6)	3 (6)	2 (4)	0
Patients with injection-site reaction — no. (%)	7 (7)	7 (14)	5 (10)	1 (2)
Flare of giant-cell arteritis reported as serious adverse event — no. (%)‡	1 (1)	1 (2)§	1 (2)	1 (2)
Patients with $\geq 1$ serious adverse event — no. (%)				
Any	15 (15)	7 (14)	11 (22)	13 (25)
According to system organ class¶				
Infection or infestation	7 (7)	2 (4)	2 (4)	6 (12)
Vascular disorder	4 (4)	2 (4)	2 (4)	1 (2)
Respiratory, thoracic, or mediastinal disorder	2 (2)	1 (2)	2 (4)	2 (4)
Injury, poisoning, or procedural complication	3 (3)	1 (2)	1 (2)	0
Nervous system disorder	1 (1)	1 (2)	2 (4)	1 (2)
Cardiac disorder	2 (2)	0	0	2 (4)
Musculoskeletal or connective-tissue disorder	1 (1)	0	1 (2)	2 (4)
Gastrointestinal disorder	1 (1)	0	2 (4)	0
Cancer	0	0	1 (2)	1 (2)

\* No gastrointestinal perforations were reported, and no patients died.

† Values are reported for the entire trial population; that is, values were included for 50 patients in the group that received tocilizumab every other week (i.e., including the patient who did not receive tocilizumab).

‡ Values are for flares of giant-cell arteritis that met the protocol-defined criteria for being reported as a serious adverse event.

§ This patient had anterior ischemic optic neuropathy after randomization.

¶ Values were those reported in at least 1% of the patients overall. Patients may have had more than one class of serious adverse event.

|| One patient in the group that received tocilizumab every other week had a benign ovarian adenoma.

# Trial of Tocilizumab in Giant-Cell Arteritis (GiACTA)

## CONCLUSIONS

Tocilizumab, received weekly or every other week, combined with a 26-week prednisone taper was superior to either 26-week or 52-week prednisone tapering plus placebo with regard to sustained glucocorticoid-free remission in patients with giant-cell arteritis.

Longer follow-up is necessary to determine the durability of remission and safety of tocilizumab.

## **PI\_164 Assessing Canadian Practice Patterns Regarding Idiopathic Aortitis**

**Objectives:** Idiopathic Aortitis (IA) and its subset, Isolated Aortitis (IsA), are presently poorly defined entities. The purpose of this study is to determine the current practice of Canadian rheumatologists with respect to these conditions.

**Methods:** An online survey was administered to members of Canadian

Rheumatology Association (CRA) using FluidSurveys in June 2016. The survey was developed by the investigators in consultation with core members of Canadian Vasculitis Network (CanVasc).

## **PI\_164 Assessing Canadian Practice Patterns Regarding Idiopathic Aortitis**

**Results:** Sixty eight of the 420 (16%) members of CRA took the survey and 60/68 (88%) completed it.

Twelve participants (19%) were core members of CanVasc, 44 (69%) were academic and 20 (31%) were community physicians.

Fifteen participants (23%) had never seen a patient with IA; out of 47 respondents who saw at least one IA patient, 37 (79%) saw 0-1 patient per year, 9 (19%) saw 2-5, and one saw 6-10.

Twelve (26%) participants reported making a distinction between IA and IsA; 9/12 (75%) considered exclusion of radiographic abnormalities in aortic branch vessels to be important for the definition of IsA.

Majority of respondents performed thorough clinical, biochemical, and radiographic assessment of their patients..



## PI\_164 Assessing Canadian Practice Patterns Regarding Idiopathic Aortitis

**Results:** Still, only 42% consistently excluded tuberculosis, 78% consistently tested for syphilis, and 38% performed full imaging of chest and abdominal aortic branches.

Great variability exists with respect to managing of these conditions. When faced with an asymptomatic patient with normal inflammatory markers, participants were more likely to give corticosteroids to patients with branch vessel abnormalities (61% and 26% for aortitis diagnosed on pathology and imaging, respectively) than when disease was localized to aorta (23%-26%).

The greatest variability was seen for localized aortitis where the involved area was completely surgically removed, with 18% of respondents always using corticosteroids, 21% did sometimes and 34% never.

More than 70% of participants monitor patients with IA every three months in the first 2 years of disease.

Thirty-six of 37 participants (97%) felt that development of recommendations for the management of patients with IA would be beneficial

## **PI\_164 Assessing Canadian Practice Patterns Regarding Idiopathic Aortitis**

**Conclusions:** IA is rare, and significant proportion of Canadian rheumatologists are not familiar with it.

Great variability exists with respect to definitions, workup, treatment, and monitoring of IA, highlighting the need for systematic studies and management recommendations.

## **PI\_165 Review of cases of surgically-diagnosed aortitis at 2 Canadian centres**

**Objective:** To characterize cases of surgically-diagnosed aortitis at 2 Canadian centres over 10 years.

**Methods:** A retrospective review of all cases of aortitis diagnosed on pathologic specimens of patients undergoing cardiothoracic surgery at the University of Calgary, Calgary, Alberta and the University of Ottawa Heart Institute, Ottawa, Ontario, between January 2003 and July 2013, was performed.

## **PI\_165 Review of cases of surgically-diagnosed aortitis at 2 Canadian centres**

**Results:** Eighty-eight cases of aortitis were identified (41 in Calgary and 47 in Ottawa).

Twelve cases (14%) were infectious.

Of the 76 cases of non-infectious aortitis (NIA), 58 (76%) were idiopathic (IA) (16 of which could be further classified as isolated aortitis), and 18 (24%) were secondary (SA) (9 giant cell arteritis (GCA), 3 Takayasu's, 3 rheumatoid arthritis (RA), 2 polymyalgia rheumatica, and 1 Bechet's disease).

The source of diagnostic specimen was a thoracic aneurysm in 63/76 (83%) of NIA patients, and the majority of aneurysms (64/76, 84%) involved the ascending aorta.

Twenty eight (19 IA and 9 SA) patients had full imaging of aorta and branch vessels at follow-up.

Of those, 15 had received post-operative glucocorticoids: 7/19 (37%) IA and 8/9 (89%) SA.

## **PI\_165 Review of cases of surgically-diagnosed aortitis at 2 Canadian centres**

**Results:** New radiographic lesions developed in 6/15 (40%) treated and 6/13 (46%) untreated patients, NS.

10/12 (83%) patients with new lesions at follow up had additional aortic and/or branch lesions at the time of diagnosis of aortitis.

Seven patients were diagnosed with a systemic condition within one year of diagnosis of aortitis (4 GCA, 2 Takayasu's, 1 Bechet's), and these were analyzed as cases of SA.

Two patients were diagnosed with a new systemic condition between 6.2 and 8 years of follow up (SLE an RA, respectively).

## **PI\_165 Review of cases of surgically-diagnosed aortitis at 2 Canadian centres**

**Conclusions:** Aside from the increased prevalence of cardiovascular risk factors in IA and the expected increased use of glucocorticoids and immunosuppressive agents in SA, the two groups appear to be similar.

The majority (26/40, 65%) of patients with NIA had additional aortic and/or branch lesions at baseline, and 43% (12/28) developed new lesions at follow-up, underlining the importance of systematic vascular imaging.

Treatment with glucocorticoids does not appear to alter the risk of development of new radiographic lesions.

# Medium Vessel Vasculitis







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## **PI\_55 Association of Five Factor Score with the mortality in Japanese patients with polyarteritis nodosa**

**Objectives:** To determine mortality and its predictive factors in Japanese patients with polyarteritis nodosa (PAN).

**Methods:** The mortality of 18 patients with PAN admitted to Juntendo University Hospital from 1994 to 2016 was retrospectively examined.

Variables at baseline, including patient demographics, clinical characteristics, and treatment, were analyzed for their association with the mortality.

## The five factor score

As established based on 342 patients with polyarteritis nodosa or Churg–Strauss syndrome, and further validated in microscopic polyangiitis.

	FFS	5–year survival rate (%)	Relative risk
Proteinuria > 1 g/24 h			
Creatininemia > 140 μ mol/L	0	88.1	0.62
Specific gastrointestinal involvement	1	74.1*	1.35
Specific cardiomyopathy	≥ 2	54.1**	2.40
Specific CNS involvement			

\*p < 0.005 and \*\*p < 0.0001 as compared to patients with FFS = 0.

1 point for each of these 5 items when present

### Références

- Gayraud M, Guillevin L, le Toumelin P, Cohen P, Lhote F, Casassus P, et al. Long-term followup of polyarteritis nodosa, microscopic polyangiitis, and Churg-Strauss syndrome: analysis of four prospective trials including 278 patients. *Arthritis Rheum* 2001;44(3):666-75.
- Guillevin L, Lhote F, Gayraud M, Cohen P, Jarrousse B, Lortholary O, et al. Prognostic factors in polyarteritis nodosa and Churg-Strauss syndrome. A prospective study in 342 patients. *Medicine (Baltimore)* 1996;75(1):17-28.

## **PI\_55 Association of Five Factor Score with the mortality in Japanese patients with polyarteritis nodosa**

**Results:** The mean follow-up period was 87.7 months (range 11 - 207 months).

The mean age of onset was 54.2 years.

The five-factor scores (FFS) revised in 2009 were 0 in 8 cases, 1 in 9 cases, and 4 in one case.

All patients received daily oral or intravenous prednisolone with or without 500 or 1000 mg of daily intravenous methylprednisolone pulse therapy for 3 consecutive days.

Nine patients (50%) were treated with an immunosuppressant, i.e., cyclophosphamide, azathioprine, or cyclosporine A.

## **PI\_55 Association of Five Factor Score with the mortality in Japanese patients with polyarteritis nodosa**

**Results:** Relapse was observed in 6 patients (33.4%).

The mean survival time was 168.6 months, the 1-year survival rate was 100%, and the 5-years survival rate was 80.0%.

Three patients died during the observation period, two of them were due to PAN itself (thrombotic thrombocytopenic purpura and gastric ulcer, respectively), one was due to infection associated with immunosuppression (invasive pulmonary aspergillosis).

The relationship between mortality defined by the survival rate and each variable was evaluated by Cox univariate analysis.

Higher 2009 FFS increased mortality with a hazard ratio (HR) of 2.34 ( $p = 0.04$ ).

Relapse-free survival time was significantly associated with elevated BUN or creatinine (HR: 7.28,  $p = 0.048$ ), BVAS (HRs: 1.26,  $p = 0.02$ ), the 1996 FFS (HR: 2.32,  $p = 0.03$ ), and the 2009 FFS (HR: 1.82,  $p = 0.04$ ).

## **PI\_55 Association of Five Factor Score with the mortality in Japanese patients with polyarteritis nodosa**

**Conclusions:** Mortality, relapse-free survival time, and their predictive factors in Japanese patients with PAN were investigated.

The 2009 FFS at diagnosis was a prognostic factor for both mortality and relapse-free survival.

# Small Vessel Vasculitis







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admission ticket.



# **WSI\_I SPUTUM ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA) IN EOSINOPHILIC GRANULAMATOSIS AND POLYANGIITIS (EGPA)**

**Objectives:** Of clinically diagnosed eGPA patients only 40% are ANCA seropositive We hypothesized that ANCA-negative patients with severe respiratory involvement would present with ANCAs localized to the lungs.

**Methods:** Matched sera and induced sputum from 20 eGPA patients (diagnosis based on 4/6 criteria by the American College of Rheumatology), 11 prednisone-dependent severe eosinophilic asthmatics, and 13 healthy volunteers.

The intensity of the IIF-staining was scored by three blinded observers. Further, to negate false pANCA patterns portrayed by anti-nuclear antibodies, both ethanol, and formalin-fixed neutrophil-substrate slides, in addition to Hep-2 IIF were employed.

# WSI\_I SPUTUM ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA) IN EOSINOPHILIC GRANULAMATOSIS AND POLYANGIITIS (EGPA)

**Results:** 14 out of 20 eGPA patients (70%) showed significant increase in sputum-ANCA intensity scores compared to eosinophilic asthmatics and healthy controls (Kruskal-Wallis,  $P < 0.0001$ ).

Further, 9/11 ANCA-seronegative patients, and 5/9 seropositive patients showed sputum-ANCA reactivity.

Presence of sputum-ANCA was significantly higher in patients with clinical manifestations of severe asthma (determined by methacholine challenge test and/or bronchodilator reversibility) and/or presence of sputum eosinophilia  $>3\%$  (Chi Square,  $P = 0.01$ ).

<b>Clinical Manifestations</b> <b>(n = 20)</b>	<i>Sputum-Positive</i>	<i>Sputum-Positive</i>	<i>Sputum-negative</i>	<i>Sputum-negative</i>
	<i>Sero-negative</i>	<i>Sero-positive</i>	<i>Sero-negative</i>	<i>Sero-positive</i>
<i>Vasculitic symptoms</i>	1	0	1	4
<i>Respiratory symptoms</i>	5	0	0	0
<i>Combined</i>	3	5	1	0

Chi-Square, df 16.23, 6; P value = 0.012

S.R Thomas, M. Mukherjee, S. Davychenko, H. Lim, M. Kjarsgaard, K. Radford, D. Robins, N. Khalidi P.Nair  
 Rheumatology (Oxford) (2017) 56 (suppl\_3): iii17-iii19.

# **WSI\_I SPUTUM ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA) IN EOSINOPHILIC GRANULAMATOSIS AND POLYANGIITIS (EGPA)**

## **Results:**

In contrast to the characteristic pANCA staining in sera, sputum immunoglobulins from 12/14 sputum-ANCA-positive patients produced a cytoplasmic staining pattern (cANCA).

This further corroborated the discordance with sputum anti-MPO reactivity analysed using ELISA.

However, the two patient samples with sputum-pANCA-type staining patterns showed increased anti-MPO absorbance values (above the 90th percentile of healthy controls).

# **WSI\_I SPUTUM ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA) IN EOSINOPHILIC GRANULAMATOSIS AND POLYANGIITIS (EGPA)**

**Conclusions:** For the first time, we report ANCA reactivity in the sputum of eGPA patients in whom the disease severity is driven by respiratory rather than vasculitis complications.

The sputum-cANCA staining pattern suggests possible autoantigen targets like proteinase 3 in the lungs, investigations for which are currently ongoing.



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ORIGINAL ARTICLE

# Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis

M.E. Wechsler, P. Akuthota, D. Jayne, P. Khoury, A. Klion, C.A. Langford, P.A. Merkel, F. Moosig, U. Specks, M.C. Cid, R. Luqmani, J. Brown, S. Mallett, R. Philipson, S.W. Yancey, J. Steinfeld, P.F. Weller, and G.J. Gleich, for the EGPA Mepolizumab Study Team\*

# Mepolizumab or Placebo for eGPA (MIRRA)

## **BACKGROUND:**

Eosinophilic granulomatosis with polyangiitis is an eosinophilic vasculitis.

Mepolizumab, an anti-interleukin-5 monoclonal antibody, reduces blood eosinophil counts and may have value in the treatment of eosinophilic granulomatosis with polyangiitis.

**METHODS** In this multicenter, double-blind, parallel-group, phase 3 trial, randomly assigned participants with relapsing or refractory eosinophilic granulomatosis with polyangiitis who had received treatment for at least 4 weeks and were taking a stable prednisolone or prednisone dose to receive 300 mg of mepolizumab or placebo, administered subcutaneously every 4 weeks, plus standard care, for 52 weeks.

The two primary end points were the accrued weeks of remission over a 52-week period and the proportion of participants in remission at both week 36 and week 48.

Secondary end points included the time to first relapse and the average daily glucocorticoid dose (during weeks 48 through 52). The annualized relapse rate and safety were assessed.



## Mepolizumab or Placebo for eGPA (MIRRA)

**RESULTS** A total of 136 participants underwent randomization, with 68 participants assigned to receive mepolizumab and 68 to receive placebo.

Mepolizumab treatment led to significantly more accrued weeks of remission than placebo (28% vs. 3% of the participants had  $\geq 24$  weeks of accrued remission; odds ratio, 5.91; 95% confidence interval [CI], 2.68 to 13.03;  $P < 0.001$ ) and a higher percentage of participants in remission at both week 36 and week 48 (32% vs. 3%; odds ratio, 16.74; 95% CI, 3.61 to 77.56;  $P < 0.001$ ).

Remission did not occur in 47% of the participants in the mepolizumab group versus 81% of those in the placebo group.

The annualized relapse rate was 1.14 in the mepolizumab group, as compared with 2.27 in the placebo group (rate ratio, 0.50; 95% CI, 0.36 to 0.70;  $P < 0.001$ ).

A total of 44% of the participants in the mepolizumab group, as compared with 7% of those in the placebo group, had an average daily dose of prednisolone or prednisone of 4.0 mg or less per day during weeks 48 through 52 (odds ratio, 0.20; 95% CI, 0.09 to 0.41;  $P < 0.001$ ).

The safety profile of mepolizumab was similar to that observed in previous studies.

# Mepolizumab or Placebo for eGPA (MIRRA)

## CONCLUSIONS

In participants with eosinophilic granulomatosis with polyangiitis, mepolizumab resulted in significantly more weeks in remission and a higher proportion of participants in remission than did placebo, thus allowing for reduced glucocorticoid use.

Even so, only approximately half the participants treated with mepolizumab had protocol-defined remission.

## **P2\_14 Late-Onset Relapse in Patients with Systemic Vasculitis**

**Objective:** Little is known about the incidence of late-onset relapse in systemic vasculitis. This study examined the incidence of relapse  $< 2$  years and  $\geq 2$  years after diagnosis in 6 different types of systemic vasculitis.

**Methods:** Data from patients in the Vasculitis Clinical Research Consortium Longitudinal Study, a prospective, multicenter North American cohort, were included if they had no relapse between the date of diagnosis and enrollment into the cohort.

Six vasculitides were studied: granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA), giant cell arteritis (GCA), Takayasu's arteritis (TAK), and polyarteritis nodosa (PAN).

Kaplan-Meier curves of the incidence of relapse over time and incidence rates  $< 2$  years and  $\geq 2$  years from diagnosis were compared within each type of vasculitis.

## **P2\_14 Late-Onset Relapse in Patients with Systemic Vasculitis**

**Results:** There were 743 patients included in this study:

261 GPA, 95 EGPA, 57 MPA, 212 GCA, 70 TAK, and 48 PAN.

A significant decrease in the incidence rate of relapse over time was seen in MPA and GCA but not in the other types of vasculitis.

Among those who relapsed, the proportion on non-glucocorticoid immunosuppressive therapy at the time of relapse was not significantly different between the 2 time periods, except for PAN.

## **P2\_14 Late-Onset Relapse in Patients with Systemic Vasculitis**

**Conclusion:** In MPA and GCA, the incidence of relapse significantly decreases after 2 years among those who maintain remission for at least 2 years after diagnosis.

However, there are no significant differences in the incidence of relapse after 2 years in GPA, EGPA, TAK, and PAN.

Use of maintenance immunosuppressive therapy at time of relapse is not significantly different between those who relapse within or after 2 years, suggesting medication use alone cannot account for late-onset relapses.

These data indicate that continued close monitoring years after diagnosis is required in patients with systemic vasculitis.

## **P2\_132 Plasma Exchange and Glucocorticoid Dosing in the Treatment of Anti-Neutrophil Cytoplasm Antibody Associated Vasculitis: Baseline Characteristics of a Randomized Controlled Trial (PEXIVAS)**

**Background:** Severe anti-neutrophil cytoplasm antibody associated vasculitis (AAV) is associated with a high risk of end-stage renal disease (ESRD) and death.

Whether plasma exchange in addition to immunosuppression and glucocorticoids for treating severe AAV reduces the risk of ESRD or death is uncertain.

Additionally, the optimal dosing of oral glucocorticoids is uncertain. PEXIVAS is an international, 2-by-2 factorial, randomized controlled trial that addresses the effect of adjuvant plasma exchange and two different regimens of glucocorticoids in AAV.

## **P2\_132 Plasma Exchange and Glucocorticoid Dosing in the Treatment of Anti-Neutrophil Cytoplasm Antibody Associated Vasculitis: Baseline Characteristics of a Randomized Controlled Trial (PEXIVAS)**

**Methods:** Eligible participants had either granulomatosis with polyangiitis or microscopic polyangiitis, a positive anti-PR3 or anti-MPO ANCA and either reduced renal function (GFR < 50ml/min) or diffuse alveolar hemorrhage, or both.

Consenting participants were allocated to seven plasma exchanges or no plasma exchange and also allocated to a standard or reduced oral glucocorticoid regimen.

All participants received cyclophosphamide or rituximab.

The primary outcome was the composite of all-cause mortality or ESRD.

## **P2\_132 Plasma Exchange and Glucocorticoid Dosing in the Treatment of Anti-Neutrophil Cytoplasm Antibody Associated Vasculitis: Baseline Characteristics of a Randomized Controlled Trial (PEXIVAS)**

**Results:** 704 participants were recruited from 95 centres in 16 countries between 2010 and 2016.

Baseline data from the first 701 participants showed a mean age of 63 years, 396 (56%) were male, 283 (40%) were PR3 positive, 182 (27%) had pulmonary hemorrhage, and 136 (19%) required dialysis.

Planned immunosuppressive treatment was IV cyclophosphamide for 352 (50%), oral cyclophosphamide for 239 (34%) and rituximab for 110 (16%).

The last follow-up is expected to occur in August 2017.



## **P2\_132 Plasma Exchange and Glucocorticoid Dosing in the Treatment of Anti-Neutrophil Cytoplasm Antibody Associated Vasculitis: Baseline Characteristics of a Randomized Controlled Trial (PEXIVAS)**

**Conclusions:** PEXIVAS is the largest trial in AAV conducted to date and will inform both plasma exchange as an adjuvant therapy and oral glucocorticoid dosing. PEXIVAS results are expected in late 2017.

## **P2\_135 RITAZAREM: An international, open-label, randomised controlled trial comparing rituximab with azathioprine as maintenance therapy in relapsing ANCA-associated vasculitis**

**Objectives:** Over 50% of patients with ANCA-associated vasculitis will experience a relapse of disease within 5 years of diagnosis.

The RAVE and RITUXVAS trials showed rituximab to be equivalent to cyclophosphamide for induction of remission in newly-diagnosed patients, and superior for those with relapsing disease.

The MAINRITSAN trial showed that repeat dosing of rituximab is superior to azathioprine for the maintenance of remission following induction with cyclophosphamide in a population of predominantly newly-diagnosed individuals.

The RITAZAREM trial aims to address the following important unanswered questions: Is a treatment regimen of fixed-interval repeat dosing of rituximab superior to azathioprine for the prevention of disease flare in AAV following rituximab induction therapy in a study population entirely made up of patients with relapsing disease?

How durable are remissions beyond the 24-month treatment period following treatment with either rituximab or azathioprine?

## **P2\_135 RITAZAREM: An international, open-label, randomised controlled trial comparing rituximab with azathioprine as maintenance therapy in relapsing ANCA-associated vasculitis**

**Methods:** 190 patients will be enrolled and all will receive remission-induction with rituximab (4 × 375 mg/m<sup>2</sup>) and glucocorticoids.

At least 160 patients in remission at 4 months (BVAS/WG less than or equal to 1 and glucocorticoid dose less than or equal to 10 mg daily) will be randomised 1:1 to receive repeat rituximab (total dose 5g) or azathioprine (2 mg/kg/day) for a total treatment period of 24 months.

Methotrexate or mycophenolate mofetil are options for patients intolerant of azathioprine

The RITAZAREM trial is directed by the European Vasculitis Society (EUVAS) and the Vasculitis Clinical Research Consortium (VCRC) and funded by Arthritis Research UK, the US National Institute of Arthritis and Musculoskeletal and Skin Diseases, Roche, and Genentech.

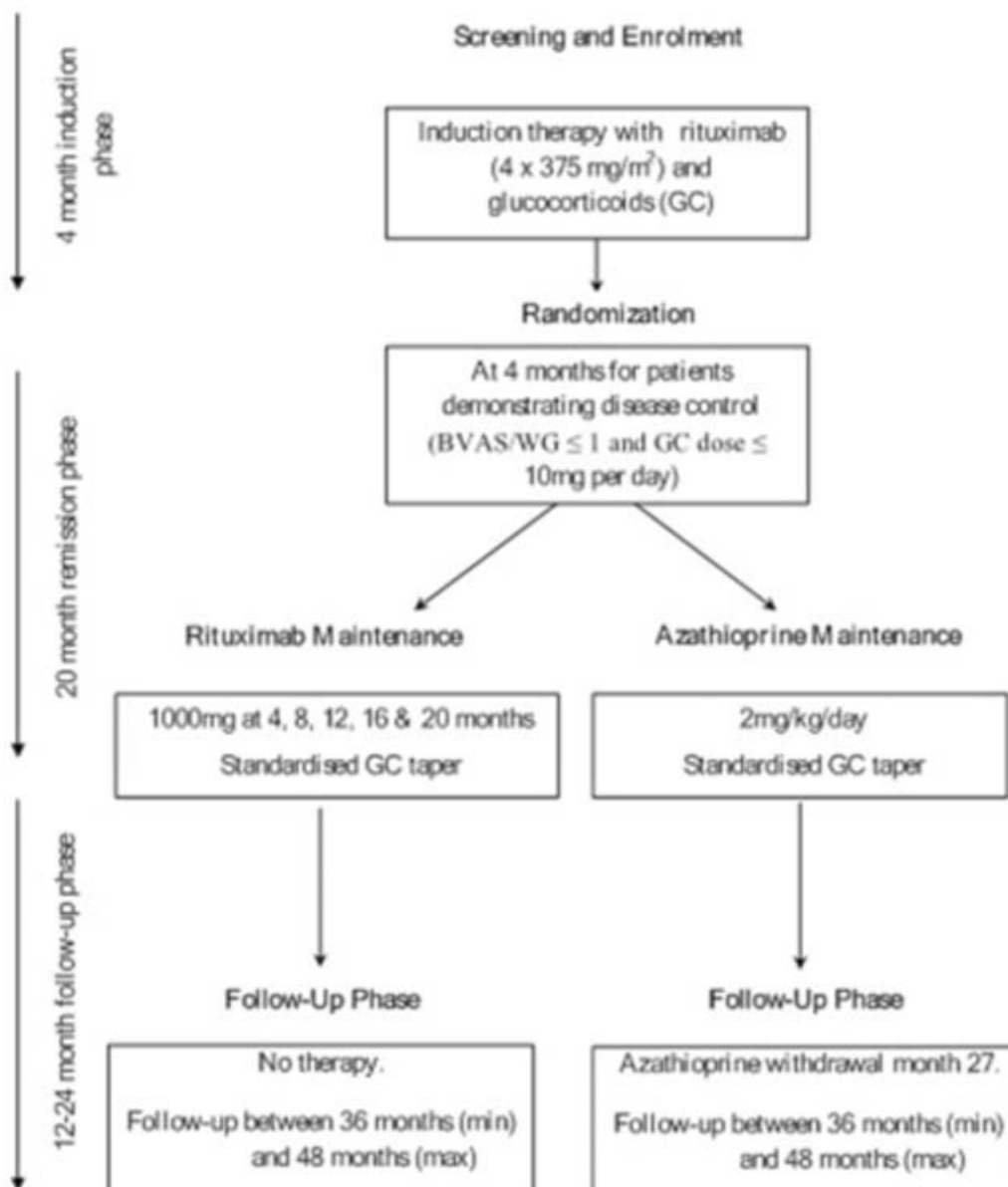
## **P2\_135 RITAZAREM: An international, open-label, randomised controlled trial comparing rituximab with azathioprine as maintenance therapy in relapsing ANCA-associated vasculitis**

**Results:** As of October 30, 2016, 186 patients had been recruited from 38 sites.

156 patients had been randomised into the maintenance phase of the trial.

18 failed to meet criteria for randomisation; the remaining 12 patients are still in the 4-month induction period.

Figures: RITAZAREM Trial Flow Chart



**P2\_135 RITAZAREM: An international, open-label, randomised controlled trial comparing rituximab with azathioprine as maintenance therapy in relapsing ANCA-associated vasculitis**

**Conclusions:** Data generated in this study will complement existing retrospective cohort data and the recently-published MAINRITSAN data, and address the question of the optimal maintenance strategy following rituximab induction therapy for patients with AAV.

# In Conclusion...

1. PET/CT scan is promising in Takayasu's – more study is needed
2. Abatacept is not effective in Takayasu's – Actemra and Rituximab are promising
3. Abatacept and Tocilizumab are effective in GCA
4. Mepolizumab is effective in eGPA
5. PEXIVAS results are pending – SOON
6. Rituximab as maintenance agent is gaining evidence





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