Clinical Updates in the Treatment of Giant Cell Arteritis: Highlights From Washington, DC

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Activity Information

Expert commentary is based on data presented at a recent rheumatology conference.

Activity Description and Educational Objectives
In this activity, a distinguished rheumatologist discusses new findings in giant cell arteritis that were presented at the 2016 American College of Rheumatology/Association of Rheumatology Health Professionals Annual Meeting in Washington, DC.

Upon completion of this activity, participants should be better able to:
- Apply approaches to treat patients with giant cell arteritis in the context of patient-, disease-, and therapy-related factors
- Discuss emerging data for the efficacy and safety of approved and investigational giant cell arteritis treatments, as well as the potential clinical impact of these findings

Target Audience
This activity has been designed to meet the educational needs of rheumatologists, ophthalmologists, neurologists, and other clinicians involved in the treatment of patients with giant cell arteritis.

Requirements for Successful Completion
In order to receive credit, participants must view the activity and complete the post-test and evaluation form. A score of 70% or higher is needed to obtain CME credit. There are no pre-requisites and there is no fee to participate in this activity or to receive CME credit. Statements of Credit are awarded upon successful completion of the post-test and evaluation form.

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Clinical Updates in the Treatment of Giant Cell Arteritis: Highlights From Washington, DC

New Horizons in the Treatment of Giant Cell Arteritis

Dr. Stone: Hello, I'm Dr. John Stone, Professor of Medicine at Harvard Medical School. I'm the Edward A. Fox Chair in Medicine and Director of Clinical Rheumatology at the Massachusetts General Hospital in Boston. Welcome to this educational activity focused on updates in giant cell arteritis that were presented at the American College of Rheumatology 2016 Annual Meeting. After completing the activity, please access the post-test and evaluation form by clicking the red "Get Certificate" button. I encourage you to download the slides, Practice Aids, and any other activity features that may interest you.

Introduction

High-dose steroids—the cornerstone of treatment for patients with GCA—often fail to control disease in the long term; chronic steroid use is associated with complications in the majority of these patients.

Unfortunately, patients with GCA have not had much choice but to be treated with steroids due to the risk of blindness, stroke, and aortic aneurysms without them. There have not been new treatments for giant cell arteritis in more than 50 years; however, a variety of agents are under investigation for this disease and the treatment paradigm for GCA may be transformed in the near future. Data for some of these therapies were presented at the 2016 ACR/ARHP Annual Meeting in Washington, DC.

GiACTA Study Design


GiACTA is a global, randomized, double-blind, placebo-controlled phase 3 trial evaluating the efficacy and safety of this agent in the treatment of GCA. At ACR, I presented data from GiACTA for up to week 52, the time of primary outcome measurement.

Let’s begin by discussing tocilizumab, a monoclonal antibody targeting the IL-6 receptor alpha that is currently approved for the treatment of rheumatoid arthritis and certain forms of juvenile idiopathic arthritis. In patients with GCA, IL-6 is upregulated within the inflamed arteries and in the peripheral circulation, and serum IL-6 concentrations correlate with disease activity, providing a rationale for studying tocilizumab in this disease.

High-dose steroids have been the cornerstone of treatment for patients suffering from giant cell arteritis, or GCA. However, steroids often fail to control disease in the long term and chronic steroid use is associated with complications in the majority of these patients, such as diabetes, hypertension, cataracts, and bone fractures.

Two hundred fifty-one patients across 76 sites in 14 countries were included in this study. Patients were at least 50 years old and had to have active GCA in order to be enrolled. They were randomized to receive one of four treatments: one, a short-course 26-week prednisone taper; two, a long-course 52-week prednisone taper; three, weekly tocilizumab plus a 26-week prednisone taper; or four, tocilizumab every other week with a 26-week prednisone taper. GiACTA is the largest clinical trial ever conducted in GCA and the first to use a blinded, variable-dose, variable-duration steroid regimen.

Tocilizumab also had a significant steroid-sparing effect in this study. The median cumulative steroid exposure in both tocilizumab groups was less than half that of the long-course prednisone group. The incidence of adverse events was similar among the four treatment arms. No deaths and no new vision loss occurred over the period of observation. These results imply that tocilizumab is a safe, effective option for patients with GCA and a significant portion of patients can remain in remission with tocilizumab for 6 months without any steroid use. This agent has been granted a Breakthrough Therapy Designation by the FDA and hopefully will be approved sometime in 2017.

In the primary comparison, 56% of patients in the weekly tocilizumab group and 53.1% of those in the every-other-week tocilizumab group achieved sustained remission at 12 months—compared to only 14% in the short-course prednisone group. In the key secondary efficacy comparison, the percentage of patients in sustained remission in each tocilizumab group was also superior to that of patients in the long-course prednisone group, which was 17.6%.


Another study presented in Washington examined the long-term outcomes of patients treated with tocilizumab following treatment termination of a phase 2 study in which patients receiving glucocorticoids were randomized to placebo or tocilizumab as add-on therapy. Twenty patients received tocilizumab, while 10 received placebo. Tocilizumab was administered every 4 weeks for 52 weeks. After that, tocilizumab was stopped and further therapy was prescribed by the treating physicians.

By week 52, all patients receiving tocilizumab were in sustained complete remission and 18 were not receiving glucocorticoids. After the last tocilizumab infusion, 11 of 20 patients relapsed, with a median time to relapse of 5 months and a range of 2 to 14 months. None of the relapsing patients experienced blindness, aortic aneurysm, or other major vascular complications.

In 6 of 11 patients relapsing after the last study infusion, tocilizumab was re-administered at a dose of 8 mg/kg of body weight in monthly intervals after a median time of 6.5 months. In 2 of 6 of these patients, tocilizumab was stopped after 4 and 6 months, respectively, with durable remission. In 1 of these 6 patients, tocilizumab was given again for 2 months, stopped in remission, yet had to be reintroduced 6 months later due to a second relapse. Therefore, clinical and serologic remission following tocilizumab for 52 weeks does not necessarily result in relapse-free survival after termination of treatment. However, the fact that 45% of patients remained in lasting remission may help design treatment protocols to determine the appropriate maintenance dosage regimens of tocilizumab after the achievement of remission.

Although tocilizumab induces and sustains clinical remission in GCA, it does not completely suppress MR signals of vessel inflammation. Whether these signals are of prognostic importance should be further determined in larger long-term studies.

Remission was obtained in all the cases, at week 4 for 90% of patients and at weeks 8 and 12 for the two others.

75% of patients met the primary endpoint (remission with a prednisone dose of ≤0.1 mg/kg/d at week 26).

By the end of week 26 (14 wk after last TCZ infusion), 25% of patients had relapsed, at a mean dose of prednisone of 6.4 ± 2.1 mg/d.

20 adverse events were considered directly related to the study, the most common being hypercholesterolemia, infections, and elevated liver function tests.

In an effort to discern more about the inflammatory signals in the vessel walls of tocilizumab-treated patients, 28 of the patients from the phase 2 study underwent magnetic resonance angiograms, or MRA, at baseline and signals in the two treatment arms were compared. At week 12, MRAs were performed in 9 patients in the tocilizumab plus glucocorticoid group, all of whom were in clinical remission, and 4 patients in the placebo plus glucocorticoid group, 2 of whom were in remission. Three patients (or 33%) in the tocilizumab plus glucocorticoid group were in complete MRA remission, compared to 1 (or 25%) in the placebo group. At week 52, there was additional improvement, but no complete remission, on MRA in 3 participants in the tocilizumab plus glucocorticoid group, resulting in a median change in the vasculitis score of -1.0 and no improvement in the remaining 2 participants in the placebo plus glucocorticoid group, resulting in a median change in the vasculitis score of -0.5.

Remission was obtained in all the cases: at week 4 for 90% of patients and at weeks 8 and 12 for the two others. Seventy-five percent of patients met the primary endpoint, which was remission with a prednisone dose of less than or equal to 0.1 mg/kg/day at week 26. By week 26—14 weeks after the last tocilizumab infusion—one-quarter of the patients had relapsed at a mean dose of prednisone of 6.4 mg/day plus or minus 2.1 mg/day. One of these relapses was limited to a slight increase in the CRP and fibrinogen levels at week 24. Steroids were briefly increased, but the primary endpoint was reached at week 26 without subsequent relapse.

Twenty adverse events were considered directly related to the study drug, the most common being hypercholesterolemia, infections, and elevated liver function tests. The results of this study indicate that four tocilizumab infusions allow rapid steroid tapering and persistent remission with a low dose of steroids after 6 months of follow-up. However, relapses can occur after tocilizumab discontinuation, and further studies are needed to identify predictive factors of relapse.
Molecular Effects of Tocilizumab

After 5-day culture, tocilizumab selectively induced a significant decrease in CXCL13 mRNA expression in cultured arteries.

No significant changes in LTα, LTβ, IL-1β, BCL-6, BAFF, or TGFβ expression were observed upon tocilizumab treatment.

Therefore, treatment with tocilizumab elicits a selective reduction of CXCL13 expression, and disruption of B-cell homeostasis may partially account for the therapeutic effects of tocilizumab in patients with GCA.


The molecular effects of tocilizumab treatment have also been studied and results were presented at this meeting. It was hypothesized that tocilizumab may disturb B-cell homeostasis and interfere with tertiary lymphoid organ—or TLO—formation. To investigate this, temporal arteries from 13 GCA patients and 8 controls were cultured with or without tocilizumab. After 5 days of culture, tocilizumab selectively induced a significant decrease in CXCL13 mRNA expression in cultured arteries. No significant changes in lymphotoxin-α, lymphotoxin-β, interleukin-1β, BCL-6, BAFF, or TGFβ expression were observed upon tocilizumab treatment. Therefore, tocilizumab treatment appears to elicit a selective reduction of CXCL13 expression, and disruption of B-cell homeostasis may partially account for the therapeutic effects of tocilizumab in patients with GCA.

Ustekinumab in GCA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre-Ustekinumab</th>
<th>Last Follow-Up</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone dose, mg, median (IQR)</td>
<td>15 (5-20)</td>
<td>5 (3.8-10)</td>
<td>.002</td>
</tr>
<tr>
<td>ESR, mm/hr, median (IQR)</td>
<td>29 (11-43)</td>
<td>12 (8-20)</td>
<td>.020</td>
</tr>
<tr>
<td>CRP, mg/L, median (IQR)</td>
<td>12.9 (5.3-42)</td>
<td>4.5 (2-14)</td>
<td>.001</td>
</tr>
<tr>
<td>BVAS, median (IQR)</td>
<td>1 (0-2)</td>
<td>0 (0-0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stopped glucocorticoids, n (%)</td>
<td>—</td>
<td>5 (20)</td>
<td>—</td>
</tr>
<tr>
<td>Stopped other immunosuppressant, n (%)</td>
<td>—</td>
<td>15 (94)</td>
<td>—</td>
</tr>
</tbody>
</table>


Another antibody under investigation for GCA treatment is ustekinumab, which inhibits IL-12 and IL-23 by binding to their common p40 subunit. IL-12 and IL-23 stimulate Th1 and Th17 responses, respectively, both of which are believed to be important in GCA pathogenesis. At ACR, a prospective, open-label study of ustekinumab use in 25 patients with refractory GCA was presented. The median duration of ustekinumab treatment at last follow-up was 15 months. The median steroid dose decreased significantly from 15 mg at baseline to 5 mg with ustekinumab treatment. Seven patients with large vessel vasculitis had follow-up imaging with improvement of wall thickening in all and no new stenoses or aneurysms. No patients experienced a relapse during treatment.

Eleven adverse events were recorded, including two respiratory tract infections and one case each of pancreatitis with an infected pseudocyst, Bell’s palsy, thyroid goiter, alopecia, paraesthesia, tinea pedis, urinary tract infection, dental abscess, and cold extremities. Three patients discontinued ustekinumab due to adverse events or personal preference. Two subsequently had flares of polymyalgia rheumatica. These results highlight the potential of ustekinumab in the treatment of giant cell arteritis. Further study of this agent in a clinical trial is warranted.

Methotrexate: Effect on Relapse Rates in GCA

Another treatment for GCA with data presented in Washington was methotrexate. One study explored the effect of methotrexate on relapse risk and glucocorticoid use through a retrospective review of patients diagnosed with GCA from 1998 to 2013. A total of 84 patients with GCA receiving methotrexate were identified and compared to 84 patients with GCA receiving only prednisone.

Prior to methotrexate initiation, the observed relapse rate was 11.8 relapses per 10 person-years. This decreased to 3.69 relapses per 10 [person]-years following the initiation of methotrexate, a rate ratio of 0.31. In the control group, the relapse rate was 3.42 relapses per 10 [person]-years before the index date, and 2.27 relapses per 10 person-years following the index date, a rate ratio of 0.66. Although both groups had a reduction in relapse rate, the rate of decrease in relapse rate was significantly greater for patients receiving methotrexate.

The effect of methotrexate on relapse rates in GCA patients was also examined in an inception cohort of 168 patients followed at an outpatient clinic in Spain. The median number of relapses was 1, with a median lag time of 1.8 years. After adjusting for age, gender, glucocorticoids, and calendar time, exposure to methotrexate in the first month was associated with a lower risk of relapses compared to nonexposure—whereas exposure to methotrexate after the first month of diagnosis did not achieve statistical significance. Therefore, early treatment with methotrexate appears to reduce the risk of relapse in patients with GCA.

A study of the use of imaging following short-term high-dose steroid treatment was also presented at this meeting. PET/CT scans are increasingly used to diagnose large-vessel GCA. However, PET/CT is not always readily available, which may lead the clinician to either delay steroid treatment—thereby increasing the risk of GCA-related complications—or to initiate treatment at the risk of lowering the diagnostic sensitivity of PET/CT. Therefore, evidence of a possible PET/CT diagnostic window after the initiation of steroid treatment is needed.

In this study, 20 treatment-naïve patients with a mean age of 69 years and PET/CT-proven large-vessel GCA were randomized to repeat the imaging test after either 3 days or 10 days of treatment with 60 mg/day of prednisone. The vascular composite score in the aorta did not decrease after 3 days, whereas a significant decrease was seen in the supra-aortic branches at 3 days and all vascular domains at 10 days. Although FDG uptake decreased in the supra-aortic branches after 3 days, large-vessel GCA could still be diagnosed accurately in all patients. In contrast, large vessel GCA could only be diagnosed in 5 of 10 patients after 10 days. These observations suggest that for large-vessel GCA, diagnostic properties remain within the first 3 days of steroid treatment. Therefore, if PET/CT is not readily available, steroids can be initiated and the diagnosis can be confirmed within 3 days, avoiding the risks associated with delaying treatment in a patient with GCA.

So far, we've reviewed updates in the treatments for patients with GCA. Stay tuned for the next segment, where I will discuss studies exploring the use of biomarkers in the diagnosis and prognosis of GCA.
Updates in the Use of Biomarkers in the Management of Giant Cell Arteritis

Introduction

No diagnostic or prognostic markers are yet known for GCA

Due to the fact that imaging tests may not be readily available, the use of biomarkers and laboratory tests would be highly valuable

Many studies investigating the use of biological markers in GCA were presented at ACR


Dr. Stone: No diagnostic or prognostic markers are yet known for GCA. Due to the fact that imaging tests may not be readily available, the use of biomarkers and laboratory tests would be highly valuable. Many studies investigating the use of biological markers in GCA were presented at the 2016 ACR meeting.

Utilization of Acute Phase Proteins and Biomarkers

<table>
<thead>
<tr>
<th>Name of Biomarker, Cat-Off</th>
<th>Median (IQR) GCA</th>
<th>Median (IQR) Non-GCA</th>
<th>P</th>
<th>Diagnostic Sensitivity (% Positive in Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAA, 6.4 g/L</td>
<td>205.3 (26-474), N = 93</td>
<td>23.2 (0.0-220.5), N = 30</td>
<td>&lt; .001</td>
<td>98.9</td>
</tr>
<tr>
<td>CRP, 5 g/L</td>
<td>65 (5.0-123), N = 95</td>
<td>14.5 (5.0-56), N = 42</td>
<td>&lt; .001</td>
<td>99.9</td>
</tr>
<tr>
<td>Haptoglobin, 2 g/L</td>
<td>4.9 (0.4-4.2), N = 82</td>
<td>3.0 (1.4-4.25), N = 17</td>
<td>&lt; .001</td>
<td>98.3</td>
</tr>
<tr>
<td>Fibrinogen, 3.5 g/L</td>
<td>7.6 (2.3-5.5), N = 56</td>
<td>6.3 (1.5-8.2), N = 15</td>
<td>.155</td>
<td>98.3</td>
</tr>
<tr>
<td>Ferritin F 120, M 300, ng/mL</td>
<td>331 (105-462), N = 86</td>
<td>271 (151-627), N = 39</td>
<td>.074</td>
<td>69.3</td>
</tr>
<tr>
<td>Hemopexin, 1.15 g/L</td>
<td>1.4 (1.2-1.5), N = 43</td>
<td>1.2 (1.1-1.3), N = 15</td>
<td>.005</td>
<td>90.7</td>
</tr>
<tr>
<td>Orosomucoid (α1-acid glycoprotein), 1.2 g/L</td>
<td>2.0 (1.6-2.6), N = 43</td>
<td>1.5 (1.0-1.7), N = 15</td>
<td>.005</td>
<td>99.3</td>
</tr>
<tr>
<td>Albumin, 32-45 g/L</td>
<td>33 (28-36), N = 92</td>
<td>38 (34-42), N = 41</td>
<td>&lt; .001</td>
<td>43.6</td>
</tr>
<tr>
<td>IL-6, 4 ng/L</td>
<td>22.5 (7.0-42.3), N = 90</td>
<td>7 (1.0-16.5), N = 30</td>
<td>.002</td>
<td>71.1</td>
</tr>
<tr>
<td>ESR F 21, M15, mm/h</td>
<td>81 (50-105), N = 95</td>
<td>44 (25.7-76.3), N = 42</td>
<td>&lt; .001</td>
<td>97.9</td>
</tr>
<tr>
<td>Leucocytes, 10x10^9/L</td>
<td>9.2 (7.1-11.1), N = 95</td>
<td>6.1 (6.0-9.7), N = 42</td>
<td>.041</td>
<td>38.9</td>
</tr>
<tr>
<td>Thrombocytes, 360x10^9/L</td>
<td>282 (207-443), N = 93</td>
<td>283 (217-546), N = 42</td>
<td>&lt; .001</td>
<td>57.9</td>
</tr>
<tr>
<td>PCT, 0.5 mcg/L</td>
<td>0.08 (0.04-0.13), N = 56</td>
<td>0.07 (0.04-0.71), N = 17</td>
<td>.001</td>
<td>3.6</td>
</tr>
</tbody>
</table>

*There was no statistical difference in ALP between those with positive and negative biopsies.


For example, a cross-sectional study was conducted to measure serum levels of 40 selected biomarkers in 95 patients with GCA and 42 non-GCA subjects, and to determine the associations of the biomarkers with GCA diagnosis, clinical complications, and disease relapse. The acute phase proteins serum amyloid A, C-reactive protein, haptoglobin, ferritin, hemopexin, orosomucoid, and albumin all showed significant associations with a diagnosis of GCA—in addition to elevated erythrocyte sedimentation rate, white blood cell count, and platelet count. The highest diagnostic value was observed for serum amyloid A and C-reactive protein, both 98.9%, followed by erythrocyte sedimentation rate, at 97.9%.

Patients with visual disturbances had significantly lower levels of serum amyloid A, C-reactive protein, haptoglobin, and erythrocyte sedimentation rate—as well as higher levels of VCAM-1—compared with patients who did not have visual disturbances. VCAM-1 was also significantly associated with extracranial artery disease. GCA patients who relapsed during follow-up had significantly higher levels of serum amyloid A, C-reactive protein, erythrocyte sedimentation rate, and white blood cell counts at baseline. These data imply that testing multiple acute phase proteins with additional blood parameters and biomarkers can optimize earlier diagnosis, as well as predict relapse and complications such as visual disturbances and extracranial artery involvement.

Laboratory Tests for the Diagnosis of GCA

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Positive Biopsy</th>
<th>Negative Biopsy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ESR</td>
<td>58.6</td>
<td>40.1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Mean CRP</td>
<td>91.1</td>
<td>50.3</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Mean platelet count</td>
<td>424</td>
<td>334</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>


Another study examined the correlation between C-reactive protein, erythrocyte sedimentation rate, platelet count, and alkaline phosphatase with the results of temporal artery biopsy in a retrospective analysis of 422 patients. Although temporal artery biopsy is the gold standard for diagnosis of giant cell arteritis, it is not always readily available and reliability can be reduced by steroid treatment and the presence of skip lesions in the blood vessel wall. In this study, a positive biopsy was associated with increased C-reactive protein, erythrocyte sedimentation rate, and platelets. Therefore, laboratory correlates of inflammation remain as good predictors of a positive temporal artery biopsy.
Since enhanced platelet activation is a marker of inflammatory arthritis, it was hypothesized that GCA might also be associated with platelet hyperactivity, supporting the rationale for aspirin use in GCA. A study testing this hypothesis was presented at ACR. One hundred twenty-two participants were included in the study—70 with GCA and 53 healthy controls. There was no difference in soluble glycoprotein VI—a marker of platelet activation—between the two groups. In addition, there was also no association between platelet activation and disease activity or cranial ischemic complications in GCA. These findings, therefore, do not support the use of aspirin in the treatment of GCA.

A prospective study was undertaken to explore the potential impact of antiphospholipid antibodies on the clinical presentation of GCA. Antibody tests were conducted in 97 of 115 patients during the 56-month observation period. Results shown at the meeting indicated that GCA patients with at least two antiphospholipid antibodies were more likely to have severe visual manifestations—that is, transient and permanent vision loss—at presentation, as well as symptoms and ultrasonographic signs of large vessel vasculitis compared to those without antiphospholipid antibodies.

At least 1 year of follow-up data were available for 71 patients. Nearly one-half of patients relapsed during follow-up, but relapses were not associated with antiphospholipid antibody positivity at presentation in this study. These findings suggest that antiphospholipid antibodies could identify a subgroup of GCA patients with severe visual manifestations and extracranial large-vessel disease.

Subjects with GCA and negative biopsies had significantly higher pERM intensity scores compared to subjects without GCA. A study validating a ROCK activity score in a large cohort of GCA patients was presented in Washington. Biopsies of 36 subjects diagnosed with GCA despite a negative temporal artery biopsy were identified and compared to biopsies of 43 subjects without GCA. The biopsies were stained for phosphorylated ezrin/radixin/moesin—or pERM, a surrogate of ROCK activity.

Subjects with GCA and negative biopsies had significantly higher pERM intensity scores compared to subjects without GCA. Therefore, pERM staining has diagnostic significance in enhancing the sensitivity of temporal artery biopsy and helps to define the clinically important group of biopsy-negative GCA. In addition, the ROCK pathway warrants further investigation as a potential therapeutic target in GCA.

### Anti-Phospholipid Antibodies and GCA¹

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>aPL-Negative</th>
<th>≥2 aPL Abs</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient or permanent visual loss, %</td>
<td>22</td>
<td>100</td>
<td>.021</td>
</tr>
<tr>
<td>Symptoms</td>
<td>0</td>
<td>19</td>
<td>.029</td>
</tr>
<tr>
<td>Ultrasonographic signs of large vessel vasculitis</td>
<td>33</td>
<td>62</td>
<td>.054</td>
</tr>
</tbody>
</table>

49% of patients relapsed during follow-up (≥1 year) and relapses were not associated with aPL Ab positivity at presentation


### ROCK and GCA¹

<table>
<thead>
<tr>
<th></th>
<th>Non-GCA Subjects n = 43</th>
<th>TAB-Negative GCA Subjects n = 36</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pERM intensity score</td>
<td>3.9 ± 1.4</td>
<td>5.0 ± 1.4</td>
<td>.002</td>
</tr>
</tbody>
</table>

- Subjects with GCA were nearly 4 times more likely to have a high pERM intensity score compared to non-GCA subjects (OR 3.67; 95% CI, 1.19-11.36; P = .019)
- Sensitivity of high pERM intensity score for the diagnosis of GCA in histologically negative TAB was 86% (95% CI, 70-95)
- ERM staining in GCA subjects was less intense in all areas of the TAB specimens compared to the pERM staining, suggesting activation of the ROCK pathway

In conclusion, a variety of treatments are being investigated that have the potential to improve outcomes and reduce the need for steroids in patients with GCA. Further studies are needed to determine the optimal duration of treatment and maintenance dosing and further reduce the risk of relapse. Biomarkers have the potential to detect disease that is missed by imaging.

The anticipated availability of tocilizumab as a treatment for GCA will pose certain challenges for clinicians with regard to biomarkers. Tocilizumab reliably and profoundly suppresses both the erythrocyte sedimentation rate and C-reactive protein concentration, making careful history-taking, physical examination, and clinical judgment even more important parts of the disease assessment.

Well, that ends our discussion for today. I hope you've found it informative and useful. Once again, I encourage you to download the slides and Practice Aids for this activity. Don't forget to access the post-test and evaluation form by clicking the red "Get Certificate" button. Thank you very much for participating in this educational activity focused on updates in giant cell arteritis presented at ACR 2016.

**Conclusions**

- A variety of treatments are being investigated that have the potential to improve outcomes and reduce the need for steroids in patients with GCA
- Further studies may be needed to determine the optimal duration of treatment and maintenance dosing, to further reduce the risk of relapse
- Biomarkers have the potential to detect disease that is missed by imaging
- The anticipated availability of tocilizumab as a treatment for GCA will pose certain challenges for clinicians with regard to biomarkers
- Tocilizumab suppresses both ESR and CRP, making careful history-taking, physical examination, and clinical judgment even more important parts of the disease assessment

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**Genome-Wide Association Study**

Two independent signals within the HLA class II region were strongly associated with GCA

Different genetic variants of plasminogen and prolyl 4-hydroxylase subunit alpha 2, which encode proteins with relevant roles in vascular remodeling and neoangiogenesis, were also associated at the genome-wide level of significance


Data from a genome-wide association study were also presented at this meeting. Genome-wide genotypes of 2,134 patients with GCA and 9,125 unaffected controls from 10 different populations of European ancestry were collected. It was demonstrated that two independent signals within the HLA class II region were strongly associated with GCA. Different genetic variants of plasminogen and prolyl 4-hydroxylase subunit alpha 2, which encode proteins with relevant roles in vascular remodeling and neoangiogenesis, were also associated at the genome-wide level of significance. This study confirmed that HLA class II is the most relevant genetic region for GCA, and also identified novel GCA risk loci that highlight the importance of angiogenesis processes in the development of GCA.
Clinical Updates in the Treatment of Giant Cell Arteritis: Highlights From Washington, DC

Expert commentary is based on data presented at a recent rheumatology conference*
*PeerView Press is an independent publisher of conference news and medical education programs.