BSR guidelines for diagnosis and management of GCA

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- Grants from EULAR, ACR
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- Merck
- Amgen
- Mundipharma
- Servier
- GSK
- Roche
Evidence Base

- Interventions SLR GCA guidelines group
- Diagnostic SLR GCA guidelines group
- Case Vignettes GCA guidelines group
- Prognostic factors SLR GCA guidelines group
BSR and BHPR guidelines for the management of giant cell arteritis

Bhaskar Dasgupta¹, Frances A. Borg¹, Nada Hassan¹, Leslie Alexander¹, Kevin Barraclough², Brian Bourke³, Joan Fulcher⁴, Jane Hollywood¹, Andrew Hutchings⁵, Pat James⁴, Valerie Kyle⁶, Jennifer Nott⁷, Michael Power⁸ and Ash Samanta⁹ on behalf of the BSR and BHPR Standards, Guidelines and Audit Working Group

Key words: Guidelines, Giant cell arteritis, Temporal arteritis, Vasculitis Diagnosis, Management, Temporal artery biopsy, Glucocorticosteroids.

Executive summary The guidelines
2016 Guideline revision group

- Voting panel formed by rheumatologists, specialists in internal medicine, ophthalmologists, neurologists, geriatricians, general practitioners (GPs), health care professionals, patients’ representatives, methodologists and statisticians
- Literature review team formed by rheumatologists, methodologists and research fellows.
Guideline Panel

- Responsible for the formulation of the PICO (=Population, Intervention, Comparator, Outcome) questions, for the rating of the overall quality of evidence and for the formulation of the recommendations.
- Met after ANCA workshop 2015, EULAR 2015, ACR 2015, Study Groups, Webinars
- The literature review team was responsible, together with the principal investigator (PI) for the design and conduct of the systematic literature review (SLR) as well as for the synthesis of the evidence report.
Areas covered

• Need for guideline revision
• Overarching principles
• Fast Track strategies
• Diagnostic challenge and Role of Imaging
• 2016 Treatment recommendations
Need for guideline revision

- Ischemic burden of GCA and sight loss
- Wide variations of care
- Need to assimilate progress made in key areas such as imaging and therapy
- NICE accredited BSR recommendations for GCA will have a significant impact on clinical decision-making, reduce practice variations
- Highlight the research agenda where there is current lack of adequate evidence.
• Provide user-friendly, evidence-based recommendations that offer best clinical advice for diagnosis of GCA
• Short and long term management of patients with a diagnosis of GCA in a primary and secondary care setting.
• These recommendations aim at improved outcome of GCA patients
• based on best clinical evidence, alongside expert consensus.
• The recommendations take into account patient choice and informed decision-making.
Target population

- **Part 1 (diagnosis):** The target population is patients with suspected GCA.
- Construct case vignettes/clinical scenarios that are associated with different (pre-test) probabilities for GCA.
- **Part 2 (management):** The target population is patients with a diagnosis of GCA or patients with a high suspicion of GCA for initial and maintenance treatment.
- Not limited to GCA related temporal (cranial) arteritis
- Includes (extra-cranial) large vessel vasculitis (LVV) and single-organ large vessel arteritis/aortitis with or without associated PMR.
Target population

Prevalence and degree of phenotypic overlap
- Headache
- Temporal artery abnormality
- Visual disturbance/loss
- Jaw claudication/tongue pain

Localisation of inflammation
- Bilateral shoulder/hip pain
- Morning stiffness
- Peripheral arthritis/RS3PE

Imaging examples

Cranial GCA
Large-vessel GCA
PMR
<table>
<thead>
<tr>
<th>Original criteria</th>
<th>Suggested expansion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at disease onset &gt;=50 years</td>
<td>Age at disease onset &gt;=50 years</td>
</tr>
<tr>
<td>New onset headache of or new type of localized pain in the head</td>
<td><strong>Any of the following:</strong></td>
</tr>
<tr>
<td></td>
<td>• New onset headache of or new type of localized pain in the head</td>
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<tr>
<td></td>
<td>• <strong>Visual symptoms, sight loss</strong></td>
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<tr>
<td></td>
<td>• Polymyalgia rheumatica</td>
</tr>
<tr>
<td></td>
<td>• Constitutional symptoms</td>
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<td></td>
<td>• Jaw/tongue claudication</td>
</tr>
<tr>
<td>Abnormality of temporal artery</td>
<td>Abnormality of temporal and/or extra-cranial arteries</td>
</tr>
<tr>
<td>(tenderness to palpation or decreased pulsation unrelated to arteriosclerosis)</td>
<td>(tenderness to palpation or decreased pulsation, <strong>bruits of extra-cranial arteries</strong> unrelated to arteriosclerosis)</td>
</tr>
<tr>
<td>ESR ≥50mm/hour</td>
<td>ESR ≥50mm/hour and/or</td>
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<td><strong>CRP levels ≥10mg/L</strong></td>
</tr>
<tr>
<td>Abnormal artery biopsy</td>
<td>Abnormal artery biopsy and/or</td>
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<tr>
<td></td>
<td>abnormal imaging result</td>
</tr>
<tr>
<td></td>
<td>(ultrasound, MRI and/or <strong>18F-FDG-PET</strong>)</td>
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</tbody>
</table>
Target users of the guideline

- Primary, secondary and tertiary care physicians
- i.e. general practitioners, rheumatologists, ophthalmologists, neurologists and geriatricians and other specialists in general (internal) medicine
- allied health professionals such as optometrists, practice nurses, pharmacists.
Overarching principles

• fundamental aspects of clinical care
• not directly resulted from SLR, but are consensus based
• Intended as a framework for implementation of specific treatment recommendations
GCA is an emergency, GP education and public awareness strategies to recognize GCA early

- GCA is an emergency because of an increased risk of ischemic vascular complications such as blindness.
- Fast-track strategies should be implemented for an early diagnosis and therapy of GCA.
- Education of primary and secondary care professionals
- as well as public awareness enable earlier recognition of GCA symptoms reducing the ‘symptom to diagnosis and treatment’ lag
Sight loss in GCA and the fast track pathway

• The challenge
• The solution
• Evidence of improved outcomes (clinical, patient experience, financial)
• Next steps
• What you learned from the experience/what you would do differently/tips
Case Study

Southend University Hospital NHS Trust
Preventing blindness by fast-tracking suspected Giant Cell Arteritis patients to immediate treatment

Outstanding Best Practice
Service Performance and Outcomes

• On introduction of the FTP, the proportion of patients suffering from **sight loss dropped significantly from 37% to 9%** when compared with the conventional pathway.\(^1\)

• A reduction in the time from referral to rheumatology review was likely a major driving force behind the improved clinical outcomes observed, with **79% of patients ultimately diagnosed with GCA seen within one working day.**\(^1\)

• Patients referred using the FTP were diagnosed 2–3 days sooner than those in the conventional pathway, limiting exposure to precautionary high-dose steroids associated with debilitating side-effects.\(^1\)

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Financial Performance and Outcomes

• Implementation of the FTP was associated with **cost-savings** to the Trust, with a reduction in the average overall cost of diagnosing and treating a patient with suspected GCA from £2.6k to £2.2k per patient.

• In a cost-effectiveness analysis to compare the FTP with the conventional pathway, patients gained on average **2.6 quality-adjusted life years** (QALYs) by avoiding the complication of sight loss.

• The economic evaluation determined that the FTP **dominated the conventional pathway** (−£840 per QALY).
Patient Focus and Satisfaction

• The FTP aims to ensure improved public and professional awareness of GCA, conduct rapid specialist reviews and initiation of treatments, with the aim to improve patient care by preventing visual loss and unnecessary exposure to potential harmful treatment.

• Clearly defined referral pathways and well-coordinated teams ensure that care is patient-centred.

• Demonstrable close links with patient groups and uniform backing from for the FTP.

• Improved recruitment to GCA-related trials including GIACTA and SIRRESTA.

• Public education initiatives to improve awareness including through PMRGCAuk, Fight for Sight and ARMA.
Commissioning Implications

- **Secondary prevention** (King’s Fund 2013 Commissioning Priority¹) – the FTP demonstrates a significant improvement in the number of patients who suffer sight-loss as a result of an avoidable complication of GCA.

- **Care co-ordination through integrated health and social care teams** (King’s Fund 2013 Commissioning Priority¹) – improved communications between primary and secondary care ensure patients are referred quickly and appropriately.

- **Effective medicines management** (King’s Fund 2013 Commissioning Priority¹) – through timely referral and diagnosis, patients avoid unnecessary side-effects of high-dose steroids.

- **Managing urgent and emergency activity** (King’s Fund 2013 Commissioning Priority¹) – through working closely with GPs and committing to advancing the education around GCA, referrals into secondary care are more streamlined and appropriate. Furthermore, the FTP allows early diagnosis of serious non GCA pathology that may mimic GCA

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Service Pathway

- The FTP is focused on primary care and Accident & Emergency (A&E) as these are the services that regularly receive GCA referrals.

- **Patients with features of GCA without ischaemic symptoms:** referrer starts high-dose steroids and contacts the rheumatology team for review in the GCA clinic within one working day.

- **Patients with features of GCA and ischaemic symptoms:** referred to A&E for assessment, receiving advice from both Ophthalmology and Rheumatology specialties. After exclusion of other serious pathology, the patient receives GC treatment followed by further diagnostic tests.
Next steps: For patients

- A patient-friendly booklet which will be available as a DVD, handout or weblink
  - which educates patients to the nature of GCA
  - discusses signs and symptoms they may experience with often the need for urgent action to prevent permanent ischaemic complications
  - explains the assessment process and pathway
  - explains the nature of various test they may undertake
Next steps: For patients

- what treatment and results they can expect and how to live with steroids and other immunosuppression
- what other support is available and how they can access it

• An online webinar talk will also be pioneered to give further education and support for GCA patients
Next steps : for clinicians

- Each different clinician (e.g., General Practitioner, Specialist Consultant, Nurse Specialist) will need support, education and training in different areas and to a different level. We envisage our toolkit to reflect the differing needs of various professional disciplines in both primary and secondary care.
Next Steps : for clinicians

- an online package consisting of documents, powerpoint presentations and webinar videos, including:
  - Education and training and questions for subjective evaluation
  - Signs and symptoms of GCA
  - Tests and investigations education particularly temporal and axilllary artery ultrasound
  - Advice and education on pathway and referral routes
  - Treatments and protocols
  - Shared-care advice and protocols
  - Support for co-morbidities that may affect or change management
  - Latest research and news
Next steps: for clinicians

• The toolkit will also allow access to for the various clinicians to book on to training sessions and study days led by Professor Dasgupta and supported by his multi-disciplinary team

• We will organise regular lectures at Time to learn GP sessions and consider a ‘Roadshow’ to disseminate the FTP.
Specialist referral vial fast track pathway

• Patients with suspected GCA should be referred to a specialist to establish the diagnosis and management plan, preferentially via a fast-track pathway.

• Patients with established GCA should be managed in shared care between primary and secondary/tertiary care.
Immediate treatment with GCs to prevent sight loss

• Patients with a suspicion of GCA, particularly those with visual symptoms, should be treated immediately with high-dose GCs to prevent sight loss.
The panel strongly recommends confirming the diagnosis of GCA either histologically (in most cases by performing temporal artery biopsy) or by imaging of temporal or extracranial arteries (e.g. ultrasound, MRI, MRA, CT, CTA, angiography, PET-CT)
Clinical evaluation of patients with suspected GCA

• All patients with suspected GCA should be clinically evaluated for characteristic signs and symptoms of the disease.
Patients ≥ 50 years of age (likelihood increasing with advancing age)

Key symptoms of GCA:
- New-type headache
- Visual symptoms (e.g. diplopia, amaurosis fugax)
- Scalp tenderness
- Jaw/tongue claudication
- Limb claudication
- Temporal artery abnormality

In association with:
- constitutional symptoms (weight loss, fatigue, fever)
- polymyalgic symptoms

Elevated ESR and/or CRP

Early recognition of GCA is essential. Irreversible ischaemic complications such as vision loss, occur almost always early, prior to glucocorticosteroid therapy.

Immediate start of glucocorticoid therapy
40-60mg prednisone equivalent daily

Urgent specialist referral
to establish the diagnosis and management plan, preferentially via a fast-track pathway

Investigations to confirm diagnosis
Imaging or biopsy

GCA confirmed
Continue glucocorticoid therapy, monitoring regularly

GCA unlikely
Rapid glucocorticoid tapering (within 2 weeks), treat alternative diagnosis
Investigations in patients with GCA

• A minimal set of investigations (including laboratory and clinical evaluations) should be obtained in all GCA patients including the assessment of relevant comorbidities and risk factors for an unfavorable disease course and drug related adverse events.

• These investigations should include exclusion of mimicking conditions.

• However, assessments should not delay initial GC treatment.
## Glucocorticoid doses
### Benefits versus side effects

Patient specific factors shifting towards a lower level of harm

<table>
<thead>
<tr>
<th>Factors</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>[20] [35] [1]</td>
</tr>
<tr>
<td>early diagnosis, low disease activity, low cumulative GC dosage, healthy life style (especially cessation of smoking, low/no alcohol consumption), monitoring and treatment of risk factors and co-morbidities</td>
<td></td>
</tr>
<tr>
<td><strong>Glucocorticoid-induced osteoporosis</strong></td>
<td>[34] [37] [38] [39] [40]</td>
</tr>
<tr>
<td>sufficient vitamin D &amp; calcium intake, exercise, muscle strengthening, prescription on indication: bisphosphonates, osteoanabolic drugs, selective oestrogen receptor modulators</td>
<td></td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td>[42] [48] [50]</td>
</tr>
<tr>
<td>screening for infections, vaccination, usage of risk scores before therapy, follow rules of conduct (avoiding infected persons, appropriate wound care, washing hands, good sleep)</td>
<td></td>
</tr>
<tr>
<td><strong>Carbohydrate metabolism</strong></td>
<td>[54] [55]</td>
</tr>
<tr>
<td>healthy diet, appropriate exercise, weight loss for obese patients, prescription on indication: hydroxychloroquine, diuretics</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>[2] [56] [69] [71] [72] [73]</td>
</tr>
<tr>
<td>diet in low saturated fat &amp; calories, physical activity, weight normalization, sodium restriction, follow the EULAR-recommendations for cardiovascular risk management (including medications like statins or angiotensin-converting enzyme inhibitors on indication)</td>
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Strehl et al EULAR GC Task Force ARD 2016 (in press)
### Glucocorticoid doses: Benefits versus side effects

Patient specific factors shifting towards an increased level of harm

<table>
<thead>
<tr>
<th>Factors</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>high disease activity, high cumulative GC dosage, lifestyle (especially bad nutrition, smoking, high alcohol consumption)</td>
</tr>
<tr>
<td><strong>Glucocorticoid-induced osteoporosis</strong></td>
<td>age &gt; 60 years, female sex, low body weight, low bone mineral density, family history of osteoporosis, prevalent fractures, low calcium intake</td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td>age &gt; 60, male sex, comorbidities (e.g. chronic lung disease, coronary heart disease, heart failure, peripheral vascular diseases, diabetes mellitus, hepatitis C, chronic renal diseases, leukopenia, neurological disease) high number of treatment failures, prior serious infections</td>
</tr>
<tr>
<td><strong>Carbohydrate metabolism</strong></td>
<td>higher age, high BMI, genetic predisposition, long disease duration</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>higher age, male sex, severe extra-articular disease manifestation, RF positivity, ACPA positivity, comorbidities (e.g. hypertension, diabetes, dyslipidaemia, obesity, Cushing´s syndrome)</td>
</tr>
</tbody>
</table>

Strehl et al. EULAR GC Task Force ARD 2016 (in press)
<table>
<thead>
<tr>
<th>Basic laboratory dataset</th>
<th>Clinical assessments</th>
<th>Evaluation by an ophthalmologist/optometrist</th>
<th>Mimicking conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ESR and/or CRP</td>
<td>• comorbidities (e.g. hypertension, diabetes, cataract, glucose intolerance, cardiovascular disease, dyslipidemia, peptic ulcer, osteoporosis)</td>
<td>• Every patient with visual symptoms</td>
<td>Non-GCA clues include:</td>
</tr>
<tr>
<td>• blood count</td>
<td>• co-medication (e.g. NSAIDs)</td>
<td>• Every patient with risk factors for glaucoma (high myopia, presence of diabetes, family history of glaucoma)</td>
<td></td>
</tr>
<tr>
<td>• glucose</td>
<td>• risk factors for GCA related complications</td>
<td></td>
<td>• Neurological deficits (oculomotor palsy can occur with GCA)</td>
</tr>
<tr>
<td>• creatinine</td>
<td>• risk for serious infections (including performance of a chest radiograph, dipstick urinalysis and risk assessment for tuberculosis)</td>
<td></td>
<td>• Very severe constitutional symptoms</td>
</tr>
<tr>
<td>• liver function tests</td>
<td>• risk factors for other GC side effects</td>
<td></td>
<td>• Localised ENT signs</td>
</tr>
<tr>
<td>• bone profile (including calcium, alkaline phosphatase)</td>
<td></td>
<td></td>
<td>Tests at the discretion of the evaluating physicians may include:</td>
</tr>
<tr>
<td>• Chest radiograph</td>
<td></td>
<td></td>
<td>• clinical tests</td>
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<tr>
<td>• dipstick urinalysis</td>
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<td></td>
<td>• laboratory investigations (e.g. extensive serological tests such as ANA, Immunoglobulin subsets or blood tests for infections)</td>
</tr>
<tr>
<td>Additional investigations to consider:</td>
<td></td>
<td></td>
<td>• imaging</td>
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<td>• protein electrophoresis</td>
<td></td>
<td></td>
<td>• other investigations</td>
</tr>
<tr>
<td>• TSH</td>
<td></td>
<td></td>
<td>• referral to another specialist</td>
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<td>• ANCA</td>
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<td></td>
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<td>• vitamin D</td>
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Tuberculosis in high-risk groups

- People at high risk of tuberculosis
  - Information and support
  - Vaccination
    - New entrants from high-incidence countries
    - People who are immunocompromised
    - Under-served groups
    - Contacts of people with active tuberculosis

Back to overview
NICE definition of Immunocompromised

• Immunocompromised refers to a person who has a significantly impaired immune system.

• This may be because of **prolonged corticosteroid use**, tumour necrosis factor-alpha antagonists, antirejection therapy, other immunosuppressives.

• Comorbid states that affect the immune system, e.g. HIV, chronic renal disease, haematological and solid cancers, and diabetes.
Risk assessment for TB

In adults who are anticipated to be or are currently immunocompromised, do a risk assessment to establish whether testing should be offered, taking into account their:

- risk of progression to active TB based on how severely they are immunocompromised and for how long they have been immunocompromised
- risk factors for TB infection, such as country of birth or recent contact with an index case with suspected infectious or confirmed pulmonary or laryngeal TB.

For adults who are severely immunocompromised, such as those with HIV and CD4 counts of fewer than 200 cells/mm$^3$, or after solid organ or allogeneic stem cell transplant, offer an interferon-gamma release assay and concurrent Mantoux test.

- If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB (see assessing for active tuberculosis in this pathway).

- If this assessment is negative, offer them treatment for latent TB infection (see managing latent tuberculosis in this pathway).

For other adults who are immunocompromised, consider an interferon-gamma release assay alone or an interferon-gamma release assay with a concurrent Mantoux test.

- If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB (see assessing for active tuberculosis in this pathway).

- If this assessment is negative, offer them treatment for latent TB infection (see managing latent tuberculosis in this pathway).
This page discusses the recommendation for individualized management plans for GCA patients. The plan should consider co-morbidities, disease course, treatment-related adverse effects, patients' perspectives, and preferences. Treatment decisions should be made through a shared decision between the patient and the treating physician. Smoking cessation is also advised for patients.
Education of GCA patients

- Patients with GCA should have access to education on the impact of GCA and treatment (including co-morbidities and disease predictors) and advice on individually tailored exercise programs.
- This is especially because glucocorticoids have direct catabolic effects on skeletal muscles that can lead to reductions in muscle protein synthesis and protein catabolism and, ultimately, muscle weakness.
- Myopathy generally develops over several weeks to months of GC use. Patients typically present with proximal muscle weakness and atrophy in both the upper and lower extremities.
Monitoring

• Every GCA patient should be monitored with the following assessments: Risk factors and evidence for steroid-related side effects, disease complications, comorbidities, other relevant medications, evidence and risk factors for relapse/prolonged therapy.

• A continuous documentation of a minimal clinical and laboratory dataset should be conducted while prescribing GCs.
Monitoring

• Follow-up visits are suggested initially at 2, 6, 12 weeks thereafter at regular intervals for the stable patient, and in case of relapse during tapering and discontinuation of GC.

• Closer monitoring within this range is recommended for patients with an increased risk for an unfavorable disease course.

• A chest radiograph with/without echocardiography should be considered at baseline and then at 2-5 years to monitor for aortic aneurysm (echocardiography and abdominal sonography, CT, PET and MRI may also be appropriate).
Patients with GCA should have rapid and direct access to specialist advice from doctors, nurses or trained allied healthcare staff for report of any changes in their condition such as flares and adverse events.
Osteoporosis, Immunization, Infection

• The panel decided not to include PICO questions on the prevention of GC-induced osteoporosis and immunization in GCA because there are published guidelines on these issues.
• The panel recommends use of proton pump inhibitors according to individual risk factors.
• Patients without a history of chicken pox (varicella zoster virus infection) should be advised to avoid close contact with people who have chickenpox or shingles, and to seek urgent medical advice if they have been exposed.
Recommendations for Diagnosis of Suspected GCA
Figure 1

**suspected GCA\(^1\)**

- **clinical probability <20%**
  - Test\(^2\) -
  - Test\(^2\) +
  - GCA unlikely
  - **diagnosis uncertain**
  - **diagnosis re-evaluation, use of supplementary tests\(^2\)**
    - low clinical probability or other imaging method(s) do not suggest GCA
    - re-evaluate for alternative diagnoses

- **clinical probability 20-50%**
  - diagnosis uncertain
  - diagnosis re-evaluation, use of supplementary tests\(^2\)
    - high clinical probability or other imaging method(s) suggest GCA

- **clinical probability >50%**
  - Test\(^2\) -
  - Test\(^2\) +
  - treat as GCA
1. According to the clinical criteria outlined in the overarching principles.

2. Consider ultrasound of temporal and large arteries, temporal artery biopsy or other imaging methods [particularly $^{18}$F-FDG PET(-CT), CTA or MRA]
Recommendation 1 (PICO 1)

• The panel strongly recommends early investigation of patients with suspected GCA by US of the temporal and/or large arteries. The ’halo’ sign is the most important US finding suggesting GCA and the ’compression’ sign might also be considered indicative of vasculitis.

• In patients with a low clinical probability and a negative US result, a diagnosis of GCA is unlikely; these patients should be worked-up for alternative diagnoses. Patients with low clinical probability and positive or uncertain sonography should undergo further testing including temporal artery biopsy (TAB).

• Such patients may require urgent investigations for alternative serious pathology.
Recommendation 1 (PICO 1)

• In patients with an intermediate or high clinical likelihood for GCA and a negative US, TAB is also needed.

• In such cases with a positive US result, the diagnosis of GCA may be accepted and a TAB considered redundant.
The 2010 BSR/BHPR guidelines for the management of GCA, stated that imaging techniques are promising for diagnosis and monitoring of GCA,

The 2016 update makes a strong recommendation in favor of using US as a standard of care procedure that should be performed in every patient with suspected disease, particularly in a fast-track setting.
In patients with a low probability of GCA and a negative US result, the number of patients with a false negative result is acceptably low; hence TAB is not required in this group.

Although the procedural risk of biopsy is low, it is invasive and represents significant resource use. The sensitivity of temporal artery biopsy (TAB) is variable depending on the length of the specimen sampled as well as the expertise of the surgeon and the pathologist [1].
Low probability GCA

• The clinical pre-test probability of 20% (resulting in a false negative rate of 4.2% of GCA patients) was considered as the upper limit, where a negative US result might be sufficient to rule out GCA. Most cases with low probability for GCA in clinical practice, however, have a pre-test probability well below 5%, thus resulting in a false negative rate of <1%.

• Patients with negative US may need work-up for alternate diagnoses including supplementary imaging and other investigations.
In patients with an intermediate or high clinical probability and a positive US result, the low number of false positive results (3% and 1%, respectively) is also acceptable and the performance of a TAB might be considered as being redundant in this setting.

A 50% clinical probability was considered as the lower limit, where a positive US result might still be accepted without further testing, whereas patients with a low to intermediate probability (i.e. 20-50%) might always be referred to biopsy, given that neither a negative nor positive US results are sufficient to rule-out or rule-in GCA, respectively.
Prior GC therapy and US results

- Prior GC therapy may reduce the sensitivity of US results.
- There is insufficient evidence to correlate the ‘time on GCs’ with the ‘sensitivity of US’.
- Clinical experience of experts suggests that patients on GC treatment for >1 week are frequently false negative.
- Physicians should therefore not rely on negative US results alone in such cases, but consider TAB (which remains positive for several weeks), if GCA cannot be ruled out by clinical assessment.
Ultrasound equipment & training

• The panel further stressed the fact that the quality of US results strongly depend on the experience of the performing sonographer and the available US equipment. High frequency probes as well as training programs should become broadly available to physicians diagnosing and managing GCA in order to implement US as a standard of care tool in clinical practice.

• In cases, US (or other imaging methods) are not available, TAB might be considered in every patient with suspected GCA.
Recommendations on interventions
Recommendation 1 (PICO1-3)

• Panel strongly recommends immediate treatment of patients with GCA using GC within a range of 40-60mg prednisone equivalent daily.

• Within this range higher GC dose may be considered in patients with a higher body weight and/or risk factors for ischemic vasculitic complications.

• Within this range a lower GC dose may be used in patients with low body weight, absence of risk factors for ischemic vasculitic complications, particularly where comorbidities (e.g. diabetes, osteoporosis, glaucoma etc.) and/or other risk factors for GC related side effects are present.
Recommendation 1 (PICO1-3)

- The panel conditionally discourages the use of initial doses <40mg/day and >60mg/day of OP.
- In patients with recent sight loss high dose GC (e.g. 60mg prednisone equivalent daily) should be used to protect the contralateral eye.
Recommendation 2 (PICO 1-3)

• Rec 2 (PICO 4): The panel conditionally recommends GC pulse therapy with 500mg-1g i.v. MP administered for 3 consecutive days in GCA patients with visual symptoms and/or other risk factors for vasculitic ischemic complications.

• The value of GC pulse therapy in uncomplicated GCA is uncertain and must be discussed on an individual basis.
Recommendation 3 (PICO 5)

- Rec 3 (PICO 5): The panel strongly recommends individualizing dose tapering schedules, based on regular monitoring of disease control, laboratory markers and adverse events.
- The following principles of GC dose tapering are suggested:
  - initial GC dose continued until symptoms and laboratory abnormalities resolve (at least 3–4 weeks);
  - then dose is reduced by 10mg every 2 weeks to 20 mg;
  - then by 2.5mg every 2–4 weeks to 10 mg; and
  - then by 1mg every 1–2 months provided there is no relapse.
- The dose tapering needs to be individualised to recognise patient specific factors.
Relapse

- Relapse treatment:
- Return of GCA related headache should be treated with the previous higher dose of GC.
- Jaw claudication requires 60mg prednisolone.
- GCA related eye symptoms require the use of either 60mg prednisolone or GC pulse therapy.
- Symptoms of large-vessel disease should prompt further investigation with MRI or PET and the use of systemic vasculitis treatment protocols.
Recommendations 4 & 5

• Rec 4 (PICO 6+7): The panel conditionally recommends using a single daily rather than divided daily doses or alternate day doses of oral GCs for treatment of GCA.

• Rec 5 (PICO 8): No recommendation can be made for the use of modified release prednisone in the treatment of GCA.
Recommendation 6

• Rec 6 (PICO 9): The panel conditionally recommends considering an early introduction of MTX in addition to GCs in patients with risk factors for GC related adverse events, co-morbidities, and/or concomitant medications where GC related adverse events are more likely to occur.

• MTX may also be considered during follow-up of patients with a relapse, without significant response to GC or experiencing GC related adverse events.
Recommendations 7&8

• Rec 7 (PICO 10): The panel conditionally recommends against the use of Dapsone and Cyclosporine A as a GC sparing agent in GCA. No recommendation can be made for other conventional DMARDs.
The panel strongly recommends against the use of TNFα blocking agents for treatment of GCA. No recommendation can be made for other biological agents.

- Interleukin-6 blockade with Tocilizumab
- Viliger et al Lancet RCT of 30 patients
- GiACTA data awaited – RCT of 250 patients
- At ACR plenary session
Recommendation 9

- Rec 9 (PICO 12-15) The panel conditionally recommends against the routine use of aspirin, heparin, warfarin and NOACs for treatment of GCA unless it is indicated for other reasons (e.g. to treat coronary heart disease, atrial fibrillation etc).

- In special situations such as vascular ischemic complications or high risk of cardiovascular disease, aspirin may be considered on an individual basis.
Rec 10 (PICO 16) The panel conditionally recommends against the use of statins for treatment of GCA, unless it is indicated for other reasons (cardiovascular risk e.g. hyperlipidemia).
Recommendation 11

• Rec 11 (PICO 17) The panel conditionally recommends an individualised exercise program for GCA patients aimed at the maintenance of muscle mass and function and reducing falls risk.
RECOMMENDATIONS FOR AUDIT

- The key performance measure - time between onset of symptoms of GCA to initiation of glucocorticoid therapy, referral to review time, specialist review time
- Sight loss
- Minimum baseline data set recorded
- Initial GC dose and taper
- Disease monitoring frequency and outcome
- Patient reported outcomes (e.g. global Visual analogue scale, SF-36, EQ5D, fatigue), Sleep
- Cumulative GC dose, treatment related complications e.g. diabetes, fractures, infections,
- Monitoring for late complications e.g. arterial stenoses, aneurysms and their sequelae.
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