BSR and BHPR guideline for the treatment of systemic sclerosis

Christopher P. Denton, Michael Hughes, Nataliya Gak, Josephine Vila, Maya Buch, Kuntal Chakravarty, Kim Fligelstone, Luke L Gompels, Bridget Griffiths, Ariane L. Herrick, Jay Pang, Louise Parker, Anthony Redmond, Jacob van Laar, Louise Warburton, Voon H. Ong
EULAR recommendations for the treatment of systemic sclerosis: a report from the EULAR Scleroderma Trials and Research group (EUSTAR)


ABSTRACT

Purpose: The optimal treatment of systemic sclerosis (SSc) is a challenge because the pathogenesis of SSc is unclear and it is an uncommon and clinically heterogeneous disease affecting multiple organ systems. The aim of the European League Against Rheumatism (EULAR) Scleroderma Trials and Research group (EUSTAR) was to develop evidence-based, consensus-derived recommendations for the treatment of SSc.

Methods: To obtain and maintain a high level of intrinsic quality and comparability of this approach, EULAR standard operating procedures were followed. The task force comprised 18 SSc experts from Europe, the USA and Japan, two SSc patients and three fellows for training purpose. The entire set of experts, community of SSc specialists (EUSTAR members and invited experts), were considered most important in the therapy of SSc. The appropriate management of SSc patients is complex and includes issues such as early diagnosis of internal organ involvement, identification of patients who are at risk of progressive disease and non-pharmacological treatments, all of which are beyond the scope of this paper. Moreover, there are new promising therapies, as well as some established treatments, which have not yet been studied extensively enough to be included in the present set of recommendations but might be helpful in individual SSc patients. Some of these treatments are included in a separate section or research.
Best practice documents available on UKSSG page of the Scleroderma-Royal Free website.

Stand-alone publications are emerging:

- GI – published – excellent North American feedback
- Digital vasculopathy – in press
- Lung fibrosis – for submission
- Cardiac – in preparation
- Renal – in draft form

UKSSG Best practice project (2011-14)

http://www.scleroderma-royalfree.org.uk/UKSSG.html
BSR and BHPR guideline for the management of systemic sclerosis

Work started September 2012

February 2015 - submitted to BSR and first stage of external peer review – presented draft

April 2015

Target for completion September 2015

Scope and structure of draft guideline

A. General approach to SSc management
Time line for development of BSR BHPR Scleroderma Guideline

- April 2012 – invitation to develop BSR BHPR Scleroderma GL
  - September 2012 – core group invited
  - October 2012 – Conflict of Interest declarations submitted to BSR

- March 2013 – Initiation teleconference 20-3-13
  - Expansion and consolidation of the GL working group
  - April 2013 – Announcement of initiative at BSR Scleroderma SIG

- July 2013 – Teleconference to finalise strategy

- October 2013 - Teleconference to plan face-to-face meeting

- February 2014 – First Face to Face group meeting

- June 2014 – Teleconference to review progress

- October 2014 – Second Face to face meeting

  - Circulation of first draft guideline
  - Collation and harmonisation of scoring for literature reviews

- January 2015 – final draft guideline circulated in group

- February 2015 – Draft GL submitted to SAGWG at BSR
  - Reviews received – comments addressed

- April 2015 – revised GL developed and discussed at Rheumatology 2015

- Internal review and revision

- Final GL submitted for publication

- Final GL accepted for publication in Rheumatology

- May-June 2016 available on line – NICE accredited treatment for systemic sclerosis
The Scleroderma guideline ....

http://www.rheumatology.org.uk/resources/guidelines/

Submitted January 11th 2016  Accepted April 12th 2016  Published May 2016
Scleroderma guideline format

- Full guideline
- Executive summary
- Text
- Recommendations
- Figure
- Table of key studies
Part A: General approach to SSc management

Recommendations in management of early systemic sclerosis:

Early recognition and diagnosis of dcSSc is a priority with referral to a specialist SSc centre (III, C)

Patients with early dcSSc should be offered an immunosuppressive agent: MTX, MMF or intravenous cyclophosphamide (CYC) (III/C), although the evidence base is weak. Some might later be candidates for autologous haemopoietic stem cell transplant (ASCT). D-penicillamine is not recommended (IIa/C)

Autologous haemopoietic stem cell transplant (ASCT) may be considered in some cases particularly where there is risk of severe organ involvement, balancing concerns about treatment toxicity (IIa/C)

Skin involvement may be treated with either MTX (II,B) or MMF (III,C). Other options include CYC (III,C), oral steroid therapy (in as low a dose as possible to suppress symptoms, and with close monitoring of renal function; III,C) and possibly rituximab (III,C)

Azathioprine or MMF should be considered after CYC to maintain improvement in skin sclerosis and/or lung function (III,C).
Part B. Key therapies and treatment of organ based disease

Raynaud’s phenomenon (RP) and digital ulcers (DU)
Lung fibrosis
Pulmonary hypertension
Gut disease
Renal complications
Cardiac disease
Skin manifestations
Calcinosis in SSc
Musculoskeletal manifestations
Sildenafil

Prostenoids (iloprost)

**Bosentan access for severe cases**

Severe refractory disease: persistent or progressive ulceration of one or more digits causing or threatening tissue loss despite optimal treatment with vasodilators including IV prostanoids and oral sildenafil, or

Multiple DUs: 3 or more DUs either currently or occurring in the last 12 months despite IV prostanoids and sildenafil.

**Challenging process (18 months) with reduced access during development compared with previous arrangements (IFR)**

*First published: January 2015
Prepared by NHS England Specialised Services Clinical Reference Group for Specialised Rheumatology
Published by NHS England, in electronic format only.
**Recommendation for autologous stem cell transplantation in systemic sclerosis:**

Current evidence support the use of ASCT in poor prognosis diffuse SSc that does not have severe internal organ manifestations that render the treatment highly toxic (Ib, B) Final consensus 80%.

Definitive statements regarding relative safety and efficacy compared with other immunosuppressive strategies and definition of appropriate cases for ASCT will require further data (III,C) Final consensus 90%.
Agreed pathway for UK patients to be evaluated for autologous stem cell transplantation

Clinical Pathway: Autologous HSCT in poor prognosis diffuse cutaneous systemic sclerosis

Reference: NHS ENGLAND
Version 1 dated 08.09.14

Clinical Pathway:
Autologous HSCT in poor prognosis diffuse cutaneous systemic sclerosis (SSc):

Advisors: Professor Chris Denton (Rheumatology CRG), Professor John Snowden (BMT CRG), Clare Foreman (BMT CRG), Dr David Kiely (UK Pulmonary Hypertension Physicians Group), Dr Peter Lanyon (Rheumatology CRG), Sarah Watson (Rheumatology CRG)

Prepared by NHS England Clinical Reference Group for Blood and Marrow Transplantation
Recommendation for non-drug interventions in systemic sclerosis:

Although there are very few studies the opinion of the group was that non-drug interventions may be helpful in SSc and are generally not detrimental.

Specialist experience of SSc cases is likely to make non-drug interventions more effective and these approaches are popular with patients and can be expected to impact positively on the disease. More research is needed in this area (III, D) Final consensus 100%.
Part C. Service organization and delivery within NHS England

SSc must be managed within an integrated system of primary, secondary and tertiary level care.

In secondary care it is important to have a specialised multi-disciplinary team

Care should be delivered as close to a patient’s home as possible but include the essential level of SSc expertise.

Education, clinical nurse specialist-led clinic for rapid access and availability of telephone helplines form part of a recommended template for high quality care of SSc.

Additional support including self-management advice and social support should also be offered through liaison with patient-based organisations such as Raynaud’s and Scleroderma Association and Scleroderma Society.

Some services that are required are already commissioned within specialist centres including pulmonary hypertension, home parenteral nutrition, hematological stem cell transplantation and dialysis services for renal failure. These provide a template for delivery of care but it is important that specialist centres are familiar with the particular challenged posed by SSc and its multisystem nature and high burden of complications and co-morbidity.
Conclusions

Treatment of scleroderma is improving

Established treatments are being used in better ways e.g. immunosuppression

Licensed drugs are available for specific complications

Access to treatment requires co-ordinated and persistent efforts of medical teams, patients and patient organisations

Recent clinical suggest more targeted skin treatments are likely to emerge over the next few years

New scleroderma lung fibrosis trials are being planned
Acknowledgements

The authors thank the BSR audit and guidelines working group and the BSR office for help, support and encouragement in developing this guideline.