Presenter Disclosures
Janet Pope

Speaker/Advisory Board/Grants
Actelion – speaker, advisory board, trials
Bayer – advisory board, trials
Roche – advisory board, trials

Amgen, AbbVie, BMS, Celgene, GSK, Hospira, Lilly, Merck, Novartis, Pfizer, Roche, Sandofi, UCB
Objectives

- To understand how to classify and treat people living with scleroderma
- To understand how Canada has lead in this knowledge
- To answer
  - How can I get involved?
Scleroderma
A systemic autoimmune disease characterized by:
- Autoimmunity
- Immune-mediated Tissue Injury
- Chronic Inflammation
- Vascular Endothelial Injury
- Fibrosis

Key findings:
- >95% ANA positivity
- >95% Raynaud’s phenomenon

Vascular changes demonstrated by nail fold capillaroscopy
Global management of SSc is complex

Systemic sclerosis

- Fertility & pregnancy
- Daily living activities
- Sexual health
- Mental health
- Multiple organ-based complications
- Body image
- Repeated hospitalisation
- Working life
- Interpersonal relationships
- Emotional well-being
Limited cutaneous (lcSSc) vs Diffuse cutaneous Systemic Sclerosis (dcSSc)

**LcSSc**
- >95% + ANA
- Often anti-centromere
- Rare renal, heart,
- Lung involvement less common
- May develop PAH (pulmonary arterial hypertension) in long standing disease, older age

**DcSSc**
- >95% + ANA
- Often ANA nucleolar
- Scl 70 (topoisomerase1) in 30%, correlates with pulmonary fibrosis
- Renal crisis with RNA polymerase3
- May develop PAH
- Higher mortality
Who will get scleroderma?

• 1/3 of patients with Raynaud’s AND dilated capillaries OR anti-centromere antibody

• Family history is a slight risk
Autoantibodies and Microvascular Damage Are Independent Predictive Factors for the Progression of Raynaud’s Phenomenon to Systemic Sclerosis

A Twenty-Year Prospective Study of 586 Patients, With Validation of Proposed Criteria for Early Systemic Sclerosis

Martial Koenig,1 France Joyal,1 Marvin J. Fritzler,2 André Roussin,1 Michal Abrahamowicz,3 Gilles Boire,4 Jean-Richard Goulet,1 Éric Rich,1 Tamara Grodzicky,1 Yves Raymond,1 and Jean-Luc Senécal1

A

B

% of patients with normal capillaries

% of patients with no capillary enlargement

Capillary enlargement

Capillary loss

Definite SSc

Capillary telangiectases

Anti-RNAPIII

Anti-Th/To

Anti-CENP-B

Years after onset of Raynaud’s phenomenon
2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative


1Department of Internal Medicine, Aler formation, University Medical Center Utrecht, Utrecht, The Netherlands; 2Division of Dermatology, Department of Medicine, University of Toronto, Centre for Genomics and Integrative Biology, St Michael’s Hospital, Toronto, Ontario, Canada; 3Department of Medicine, University of Oxford, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, United Kingdom; 4Department of Medicine, School of Medicine, University of California, San Francisco, CA, USA; 5Department of Lifestyle Medicine, Eastern Health, Melbourne, Victoria, Australia; 6Department of Rheumatology, Academic Medical Center, Amsterdam, The Netherlands; 7Department of Rheumatology, St. Joseph’s Hospital and Medical Center, Phoenix, Arizona, USA; 8Division of Rheumatology, University of British Columbia, Vancouver, British Columbia, Canada; 9Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA; 10Department of Medicine, Centre Hospitalier Universitaire de Québec, Laval University, Quebec City, Quebec, Canada; 11Department of Medicine, Division of Rheumatology, University Medical Center, RWTH Aachen, Aachen, Germany; 12Division of Rheumatology, Mayo Clinic, Rochester, Minnesota, USA; 13Department of Internal Medicine, Division of Rheumatology, Medical Center, University of Basel, Basel, Switzerland; 14Division of Rheumatology, Department of Medicine, University of Basel, Basel, Switzerland; 15Department of Medicine, University of Medicine and Pharmacy, Poitiers, France; 16Division of Rheumatology and Clinical Immunology, Rheumato, University of Milan, Milan, Italy; 17Department of Medicine, Division of Rheumatology, University of British Columbia, Vancouver, British Columbia, Canada; 18Department of Internal Medicine, Academic Medical Center, Amsterdam, The Netherlands; 19Department of Medicine, Division of Rheumatology, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 20Department of Medicine, University of California, San Francisco, CA, USA; 21Department of Medicine, University of Washington, Seattle, Washington, USA; 22Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada; 23Department of Rheumatology, Medical University of Lodz, Lodz, Poland; 24Department of Medicine, University of Munich, Munich, Germany; 25Department of Rheumatology, University of Rome, Rome, Italy; 26Division of Rheumatology, University of Leeds, Leeds, United Kingdom; 27Department of Medicine, University of Washington, Seattle, Washington, USA; 28Department of Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA; 29Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 30Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA; 31Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 32Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 33Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 34Division of Rheumatology, Department of Medicine, University of California, San Francisco, CA, USA; 35Department of Rheumatology, University of Milan, Milan, Italy; 36Rheumato, University of Medicine and Pharmacy, Poitiers, France; 37Division of Rheumatology and Clinical Immunology, Rheumato, University of Milan, Milan, Italy; 38Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 39Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 40Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; 41Department of Internal Medicine, Aler formation, University Medical Center Utrecht, Utrecht, The Netherlands
Canadian Contributions

- Individual researchers
- Recognition of poor survival in pulmonary hypertension in Scleroderma
  - Peter Lee
- Understanding autoantibodies in Scleroderma
  - Jean Luc Senecal
  - Marv Fritzler
- Basic and Epi Scientists
  - Andrew Leask
  - Sindhu Johnson
- Registries CSRG
  - Murray Baron
  - Janet Pope
  - Marie Hudson
  - Many more
- Internet cohort SPIN
  - Brett Thombs
  - Multiple social scientists
The Scleroderma Patient-centered Intervention Network: SPIN

Brett Thombs, PhD
brett.thombs@mcgill.ca
McGill University and Jewish General Hospital
Montreal, Quebec, Canada
The 15% rule in scleroderma

15% Rule
95% have RP
80% have GERD, Dysphagia
46% have digital ulcers (ever)
15% have a current digital ulcer
   15% have a complicated digital ulcer
15% have PAH
10-15% of dcSSc have Scleroderma renal crisis (3% overall SSc)
30% have ILD/pulmonary fibrosis
   15% of pulmonary fibrosis is clinically relevant
15% have inflammatory arthritis
15% have myopathy / myositis
15% have Sjogren’s

Treatment of SSc

• Overall ‘disease modification’
• Organ specific treatment
• For some organs think about treatment of SLE
  – Induction
  – Maintenance
• Screen organs if earlier intervention improves prognosis
• Treat what is treatable
• Follow guidelines, especially if you don’t have many SSc patients in your practice
Causes of death in SSc

• ½ die of SSc related morbidity
• This is our most lethal connective tissue disease
Changes in causes of SSc-related deaths over time

Time period courtesy of Virginia Steen.

Frequency (%)


Scleroderma renal crisis
PAH
Interstitial lung disease
courtesy of Virginia Steen.
### Scleroderma Survival is Improving

10 yr survival

<table>
<thead>
<tr>
<th>Canadian Cohort</th>
<th>Limited</th>
<th>Diffuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee</td>
<td>75</td>
<td>57</td>
</tr>
<tr>
<td>1979-90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senecal</td>
<td>80</td>
<td>62</td>
</tr>
<tr>
<td>1984-99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pope</td>
<td>93</td>
<td>67</td>
</tr>
<tr>
<td>1993-2007</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Canadian Scleroderma Research Group (CSRG) Recruiting Sites

Drs Baron, Hudson, Gyger, Mathieu, Ligier & Grodzicky
Montreal, QC;
Dr. Masetto,
Sherbrooke, QC
Dr. Docherty
Moncton, NB
Dr. Sutton
Halifax, NS
Dr. Robinson
Winnipeg, MB
Dr. Markland
Saskatoon, SK
Dr. LeClercq
Calgary, AB
Dr. Pope, London &
Dr. Khalidi, Dr. Kaminska,
Hamilton, ON
Dr. Smith
Ottawa, ON
Dr. Thorne
Newmarket, ON
Drs Baron, Hudson, Gyger,
Mathieu, Ligier & Grodzicky
Montreal, QC;
Dr Masetto,
Sherbrooke, QC
Sources of funding for the CSRG

• CIHR Team Development grant
• The Arthritis Society
• Pharmaceutical companies
• Local funding for sites

• Patient organizations
  —Scleroderma Society of Canada
  —Scleroderma Society of Ontario
  —Cure Scleroderma Foundation
SSc Treatment

• Treat what is treatable
• Organ based
• Mild, moderate or severe
• Screen for common and treatable complications
  – PH
  – ILD
Improving Skin / Overall Disease

- **YES/Maybe**
- **Methotrexate**
- **Cyclophosphamide**
  - Scleroderma Lung Study
  - positive effect on skin score
- **Rituximab**
- **Mycophenylate mofetil**

- **NO**
- **Imatinib**
- **D-penicillamine**
- **Anti-TGF**
- **Relaxin Trials**
- **Tocilizumab**
- **Abatacept**
- **Antifibrotic pathways**

**Stem cell transplant**
- **SCOT**
- **ASTIS**

Daoussis D, Rheumatology. 2010;49:271
Smith V, J Rheumatol 2013;40:52
# Probability of a beneficial treatment effect from Mtx in early diffuse scleroderma

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Probability of beneficial effect in the next patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Modified Rodnan Skin Score</td>
<td>78%</td>
</tr>
<tr>
<td>UCLA skin score</td>
<td>91%</td>
</tr>
<tr>
<td>MD global assessment</td>
<td>69%</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>59%</td>
</tr>
<tr>
<td>DLCO</td>
<td>87%</td>
</tr>
</tbody>
</table>

Johnson S, et al.  
## Imatinib RCT Clinical in Scleroderma

<table>
<thead>
<tr>
<th>N=10 Total Placebo =1</th>
<th>Baseline</th>
<th>6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>51 (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>7 F : 3 M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>29 (27)</td>
<td>29 (27)</td>
<td>0.6</td>
</tr>
<tr>
<td>Months {range}</td>
<td>{1, 70}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRSS (SD)</td>
<td>32 (8)</td>
<td>30 (7)</td>
<td>0.6</td>
</tr>
<tr>
<td># with Tendon Friction Rubs</td>
<td>3</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>MD Global (0-100)</td>
<td>46 (17)</td>
<td>36 (10)</td>
<td>0.2</td>
</tr>
<tr>
<td>Patient Global (0-100)</td>
<td>66 (32)</td>
<td>39 (22)</td>
<td>0.08</td>
</tr>
<tr>
<td>HAQ (0-3)</td>
<td>1.7 (0.7)</td>
<td>1.5 (0.7)</td>
<td>0.6</td>
</tr>
<tr>
<td>Health Transition</td>
<td></td>
<td>3 much worse</td>
<td></td>
</tr>
<tr>
<td>ESR mm/hr (SD)</td>
<td>20 (19)</td>
<td>22 (25)</td>
<td>0.2</td>
</tr>
<tr>
<td>CRP (SD)</td>
<td>9 (13)</td>
<td>8 (12)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Results given as mean and (SD)
There were no between groups or within groups differences
Treatment of SSc Skin Involvement

Early dcSSc or worsening dcSSc

SSc-Related Skin Involvement

Severity?

MRSS 10
- First Line Treatment: Methotrexate (62%)
- Add (77%) • Switch (23%)
- Second Line Treatment: MMF (53%)

MRSS 24
- First Line Treatment: Methotrexate (53%)
- Add (77%) • Switch (23%)
- Second Line Treatment: MMF (43%)

MRSS 32
- First Line Treatment: Methotrexate (46%)
- Add (77%) • Switch (23%)
- Second Line Treatment: MMF (41%)

Steroid use may occasionally be considered in patients even if they are at a high risk of SRC (78%)

CRP Associations over time in Limited and Diffuse SSc

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>All Limited</th>
<th>All Diffuse</th>
<th>Early diffuse &lt;3yrs</th>
<th>Late diffuse &gt;3years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation (r): CRP vs mRSS</td>
<td>0.084</td>
<td>0.765</td>
<td>0.024*</td>
<td>0.987</td>
<td>0.009**</td>
</tr>
<tr>
<td>Correlation (r): CRP vs MD Global Assessment</td>
<td>0.872</td>
<td>0.239</td>
<td>0.084</td>
<td>0.658</td>
<td>0.176</td>
</tr>
<tr>
<td>Correlation (r): CRP vs Patient Global Assessment</td>
<td>0.661</td>
<td>0.093</td>
<td>0.434</td>
<td>0.923</td>
<td>0.301</td>
</tr>
<tr>
<td>Mean difference in CRP between Tendon Friction Rubs yes – no</td>
<td>0.013*</td>
<td>0.620</td>
<td>0.017*</td>
<td>0.149</td>
<td>0.036*</td>
</tr>
<tr>
<td>Correlation (r): CRP vs ESR</td>
<td>0.680</td>
<td>0.141</td>
<td>0.075</td>
<td>0.706</td>
<td>0.162</td>
</tr>
</tbody>
</table>

P-values for comparison of baseline and follow-up visit correlations based on 2-tailed T-test
*p<0.05, **p<0.01.
Tocilizumab vs. Placebo in active early dcSSc Improvement in Skin

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PBO 162 mg QW SC</strong></td>
<td>-1.22</td>
<td>-2.77</td>
</tr>
<tr>
<td><strong>TCZ 162 mg QW SC</strong></td>
<td>-3.92 ΔLSM (TCZ-PBO): -2.70 ( p = 0.09 )</td>
<td>-6.33 ΔLSM (TCZ-PBO): -3.55 ( p = 0.06 )</td>
</tr>
</tbody>
</table>

CI, confidence interval; LSM, least square means; ΔLSM (TCZ-PBO), difference in LSM between treatment arms. Negative change indicates improvement. Means and 95% CI are from the repeated-measures model.
Estimating Benefits from Immunesuppressive Treatment in Diffuse Cutaneous Systemic Sclerosis: Data from the Canadian Scleroderma Research Group*

Tommy Choy¹, Murray Baron², Janet E. Pope¹,³#
ASTIS Trial: Overall Survival
Autologous Stem Cell Transplant in early dcSSc

Time-dependent hazard, $p = 0.011$

10% early transplant mortality

SSc and the Lungs

Pulmonary Fibrosis
Interstitial Lung Disease

Pulmonary arterial hypertension
PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS: 
AN ANALYSIS OF 17 PATIENTS

E. T. KOH, P. LEE, D. D. GLADMAN and M. ABU-SHAKRA
University of Toronto Rheumatic Disease Unit, The Wellesley Hospital, Toronto, Ontario, Canada

Fig. 1.—Survival curves of scleroderma patients with pulmonary hypertension (n = 17), lung involvement (of all categories, n = 73) and without major organ involvement (n = 138).
Echocardiogram screening allows SSc-PAH to be detected earlier

- French registry has shown this\(^1\)
- Australian registry\(^2\)
- 13 to 16% prevalence of PAH
- **Screened patients had better 6MWD and lower PVR and more patients in FC II**

## SSc-PAH by Right Heart Catheterization

### 3.5 PAH in SSc (RHC)

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Total</th>
<th>Proportion</th>
<th>95% CI</th>
<th>W (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phung S</td>
<td>24</td>
<td>184</td>
<td>0.13</td>
<td>[0.09; 0.19]</td>
<td>9.5%</td>
</tr>
<tr>
<td>Hachulla E</td>
<td>47</td>
<td>599</td>
<td>0.08</td>
<td>[0.06; 0.10]</td>
<td>12.2%</td>
</tr>
<tr>
<td>Mukerjee D</td>
<td>89</td>
<td>722</td>
<td>0.12</td>
<td>[0.10; 0.15]</td>
<td>12.0%</td>
</tr>
<tr>
<td>Minier T</td>
<td>10</td>
<td>131</td>
<td>0.08</td>
<td>[0.04; 0.14]</td>
<td>9.8%</td>
</tr>
<tr>
<td>Joven BE</td>
<td>31</td>
<td>204</td>
<td>0.15</td>
<td>[0.11; 0.21]</td>
<td>9.4%</td>
</tr>
<tr>
<td>Hashimoto A</td>
<td>65</td>
<td>405</td>
<td>0.16</td>
<td>[0.13; 0.20]</td>
<td>10.9%</td>
</tr>
<tr>
<td>Pérez-Bocanegra C</td>
<td>61</td>
<td>319</td>
<td>0.19</td>
<td>[0.15; 0.24]</td>
<td>10.1%</td>
</tr>
<tr>
<td>Hunzelmann N</td>
<td>234</td>
<td>1483</td>
<td>0.16</td>
<td>[0.14; 0.18]</td>
<td>12.4%</td>
</tr>
<tr>
<td>Schmajuk G</td>
<td>36</td>
<td>165</td>
<td>0.22</td>
<td>[0.16; 0.29]</td>
<td>8.0%</td>
</tr>
<tr>
<td>Murata I</td>
<td>18</td>
<td>80</td>
<td>0.22</td>
<td>[0.14; 0.33]</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

**Random effects model**

- **Events**: 4292
- **Proportion**: 0.15 [0.12; 0.17] 100%

**Heterogeneity**: $I^2$-squared=84.7%, $tau^2$-squared=0.0016, p<0.0001

---

The molecular targets of approved PH therapies

HRCT: Fibrosis
ILD Treatment

Induction

Usually:
IV Cyclophosphamide (65%)

Occasionally:
1. Oral Cyclophosphamide (65%)
2. Mycophenylate Mofetil (48%)
3. Azathioprine (45%)

Maintenance

Usually:
Mycophenylate Mofetil (73%)

Occasionally:
1. Azathioprine (47%)
2. IV Cyclophosphamide (40%)
3. Oral Cyclophosphamide (32%)

Steroids are used concomitantly with other drugs when treating ILD/PF, at least initially:
Frequently (30%)
Occasionally (30%)

Interstitial Lung Disease in Scleroderma

• **Usual Treatment**
  - Cyclophosphamide
  - Mycophenylate Mofetil
  - Azathioprine

• ?Steroids

• **Experimental**
  - Tocilizumab
  - Rituximab
  - IPF treatments
ILD Progression is Related to GI Parameters: Data from CSRG

<table>
<thead>
<tr>
<th>Indicators</th>
<th>No/mild ILD vs. ILD</th>
<th>Stable vs. Progressive moderate/severe ILD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysmotility</td>
<td>∨</td>
<td>P = 0.09</td>
</tr>
<tr>
<td>PT: Difficulty Swallowing</td>
<td>∨</td>
<td></td>
</tr>
<tr>
<td>PT: Early Satiety</td>
<td>↔</td>
<td>P = 0.119</td>
</tr>
<tr>
<td>GERD</td>
<td>↔</td>
<td></td>
</tr>
<tr>
<td>PT: Food/Acid Regurgitation</td>
<td>P = 0.652</td>
<td>P = 0.072</td>
</tr>
<tr>
<td>PT: Choking at night</td>
<td>✓</td>
<td>P = 0.653</td>
</tr>
<tr>
<td>PT: Heartburn (Pyrosis)</td>
<td>✓</td>
<td>P = 0.327</td>
</tr>
<tr>
<td>Esophageal Dilatation</td>
<td>↔</td>
<td></td>
</tr>
<tr>
<td>MD: Esophageal dilatation</td>
<td>P = 0.041</td>
<td></td>
</tr>
<tr>
<td>Interaction Term</td>
<td>Dilatation*Choking</td>
<td>P = 0.263</td>
</tr>
</tbody>
</table>

In SSc with ILD, those who progress have more
Esophageal dysmotility
Choking
Need for esophageal dilation
This implies that reflux and potential aspiration should be treated aggressively
Treatment: Raynaud’s

- Cold avoidance
- Smoking cessation – no trials
- Calcium channel blockers (CCB)
- Other drugs
  - Topical or oral nitrates
    - MQX-503 a topical nitroglycerin-type medication
  - Angiotensin II blockers
    - Losarten
  - SSRI
    - Fluoxetine
  - PDE5 inhibitors
    - Sildenafil
    - Tadalafil
  - Prostacyclins
  - Alpha blockers
  - ACE do not work in RP

TIP: You should expect a 30% reduction in attacks after a couple of weeks on treatment with a calcium channel blocker. Increase dose if well tolerated and benefit is not achieved.

Thompson A. Arthritis Rheum 2001 44:1841-7
Complementary and Alternative Medicine (CAM) and RP Treatment

- 20 RCTs of CAM in RP
- In general most (CAM) trials are of poor quality
- **Laser** has positive data as does wearing therapeutic gloves but firm conclusions are not possible due to sample size or poor quality
- The other studies are negative

- acupuncture (n=2 trials),
- antioxidants (n=2),
- biofeedback (n=5),
- essential fatty acids (n=3),
- ginkgo biloba (n=1),
- l-arginine (n=2),
- laser (n=3),
- glucosaminoglycans (n=1),
- therapeutic gloves (n=1).

Tell your health care provider what you are taking. Raynaud’s can fluctuate so it may be difficult for you to know if a remedy is working.
Results of A Pilot Randomized Placebo Controlled Trial in Raynaud’s Phenomenon (RP) with St. John’s Wort (SJW)

Déanne Malenfant, Kelly Summers, N Samedi, Ash Bonner, Janet Pope

Differences between baseline and end of trial as measured as mean per day over the first and last week of treatment (t-test)
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
<th>Yes</th>
<th>No</th>
<th>All Patients</th>
<th>Diffuse SSc</th>
<th>Limited SSc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.4</td>
<td>52.9</td>
<td>57.3</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>% Males</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>% Smoked ever</td>
<td>62</td>
<td>62</td>
<td>62</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>% PAH</td>
<td>9.4</td>
<td>8.4</td>
<td>10.2</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>% Renal Crisis</td>
<td>5.3</td>
<td>5.8</td>
<td>5.0</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>% Diffuse SSc</td>
<td>43</td>
<td>55</td>
<td>38</td>
<td>✔</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Disease Duration yrs</td>
<td>13.6</td>
<td>14.7</td>
<td>12.7</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>DLCO % predicted</td>
<td>67</td>
<td>64</td>
<td>70</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>SSc age of onset</td>
<td>44.5</td>
<td>41.0</td>
<td>47.2</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>% + Topo1 (Scl-70)</td>
<td>15.1</td>
<td>24.1</td>
<td>9.4</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>% Lung disease</td>
<td>36.5</td>
<td>48.3</td>
<td>30.2</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>% Esophageal Dilatation</td>
<td>14</td>
<td>17</td>
<td>11</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Modified Rodnan Skin score</td>
<td>11.2</td>
<td>13.3</td>
<td>9.5</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>
Digital Ulcers in SSc
Digital Ulcers

- **Healing**
  - Calcium channel blockers
  - IV Prostacyclin (Iloprost)
  - Sildenafil

- **Prevention**
  - 2 RCTs with Bosentan showed reduction in new digital ulcers but no effect on healing
  - Statin
    - Atorvastatin 40mg a day
  - Possibly use of medications on healing side of this slide

Negative trials with Macitentan
SSc-related GI Involvement

SSc-Related GI Involvement

Symptomatic GI Dysmotility

Investigate?
- Always (35%)
- Frequently (23%)
- Occasionally (42%)

Ensuing Bacterial Overgrowth?
- No
- Yes

Hyperalimentation
- Frequently (37%)
- Occasionally (58%)

SSc-Related Malabsorption

Investigate with:
- Upper Endoscopy (58%)
- Barium Swallow (48%)
- Manometry (45%)

Rotate Antibiotics (100%)

PPI exceeding maximum dose:
- Frequent use (54%)

Promotility Agent:
- Frequent use (50%)

Upper Endoscopy:
- Occasional use (52%)

Barrett’s
Repeat screening

ACE inhibitor for Scleroderma Renal Crisis
Conclusions

- We can classify patients and estimate their long term outcome (prognosis)
- We need to screen for some organ involvement in scleroderma
- Canadians should be proud of the leading work in scleroderma in Canada
Search results

Items: 1 to 20 of 173
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- CIHR
- Cdn Scleroderma Society
- TAS
- CAN
- CRA
- SRTP
- Actelion
- Genentech
- Pfizer
Thank you