Current Insights on Churg-Strauss syndrome
Eosinophilic granulomatosis with polyangiitis

CanVasc: the 5 W

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Financial Interest Disclosure
(over the past 24 months)

Christian Pagnoux

<table>
<thead>
<tr>
<th>Company</th>
<th>Speaker</th>
<th>Advisory</th>
<th>Research</th>
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</thead>
<tbody>
<tr>
<td>Hoffmann-La Roche</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>GSK</td>
<td></td>
<td>✓</td>
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</table>
Objectives

• Review major characteristics of Churg-Strauss syndrome based on recent data

• Identify the unmet needs, challenges and potential future (therapeutic) developments in Churg-Strauss syndrome

• Introduce CanVasc network and objectives
Chapel Hill Nomenclature

Classification of the Vasculitides

- Arteries
  - Large
  - Small
- Arterioles
- Capillaries
- Venules
- Veins

- Aorta
- Necrotizing glomerulonephritis
- Microscopic polyangiitis
- Granulomatosis with polyangiitis (Wegener’s)
- Eosinophilic GPA (Churg Strauss syndrome)
- Polyarteritis nodosa
- Kawasaki disease
- Giant cell arteritis (Horton)
- Takayasu arteritis
- Henoch-Schoenlein purpura
- Cryoglobulinemia
- + antiGBM
- + Behçet
- + CNS-V

ANCA in EGPA

• **Positive in 35% (→ 78%) of the patients**

• Mainly **P-ANCA** (>¾ of ANCA+ patients)

• Mainly **anti-MPO** (>90% of ANCA+ patients)

*Della Rossa et al, Rheumatology (Oxford), 2002;41:1286-94
Solans et al, Rheumatology (Oxford) 2001;40:763-71*
You will very rarely see this in CSS!
ASTHMA

ASTHMA + EOSINOPHILIA

LIMITED FORMS OF CSS

CHURG-STRAUSS SYNDROME
FVSG database

383 patients with CSS/EGPA
- Mean follow-up 66.8 ± 62.5 months
- Diagnosed between 1957 and 2009
- ACR criteria and Chapel hill definitions
- 31% ANCA+ (108/348 with fresh or frozen serum samples)

Comarmond, Pagnoux et al, ANCA-WS and EULAR 2011
### Clinical manifestations

<table>
<thead>
<tr>
<th></th>
<th>All (N=383)</th>
<th>ANCA+ (N=108)</th>
<th>ANCA− (N=240)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung infiltrate</td>
<td>148 (38.6)</td>
<td>44 (40.7)</td>
<td>94 (39.2)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

*Note: ANCA stands for Antineutrophil Cytoplasmic Antibody.*
Histology

- Vasculitis features
The challenging patients...

- ANCA negative
- NO vasculitis on histology (no Bx)

→ What are the alternative diagnoses?

**ACR CLASSIFICATION CRITERIA**  
(Masi et al, 1990)

- Asthma
- Paranasal sinus abnormalities
- Mono- or polyneuropathy
- Pulmonary infiltrates, non-fixed
- Eosinophilia
- Extravascular eosinophils

4 / 6 should be present  
Se = 85%  
Sp = 99.7%
Differential diagnoses

- **HES (L-HES)** / asthma with eosinophilia
- Eosinophilic pneumonia
- Drugs / allergies
- Parasitic infections
- Lymphoma, cancer
- Other vasculitis (GPA)
IL25 in EGPA

Main source = eosinophils

n=15 (4 tested twice) ANCA+ 60%
6/6 active were ANCA+ (3 heart)
8/13 inactive were ANCA+ (61%)

Terrier et al, Blood. 2010;116:4523-31
Treatment of severe EGPA/GPA/MPA

**INDUCTION**

- **CYCLOPHOSPHAMIDE**
  - 15 mg/kg (d1,14,28 then q3wk)
  - 2 mg/kg/d
- **AZATHIOPRINE** 2 mg/kg/d
- **METHOTREXATE** 0.3 mg/kg/wk
- **LEFLUNOMIDE** 20 mg/d
- **MYCOPHENOLATE MOFETIL** 2 g/d

+ adjuvant/prophylactic measures: cotrimoxazole, osteoporosis treatment

**MAINTENANCE**

- > 18 months
  - + Corticosteroids [R]

3 - 6 months
Mepolizumab and EGPA

750 mg/month, IV

<table>
<thead>
<tr>
<th>Mean (range)</th>
<th>Week −4, enrollment</th>
<th>Week 0, treatment phase</th>
<th>Week 12, treatment phase</th>
<th>Week 16, washout phase</th>
<th>Week 20, washout phase</th>
<th>Week 28, safety-monitoring phase</th>
<th>Week 40, safety-monitoring phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone dose (mg)</td>
<td>18.8</td>
<td>12.9</td>
<td>4.6</td>
<td>6.7</td>
<td>5.0</td>
<td>4.3</td>
<td>15.7</td>
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<tr>
<td>Eosinophil (%)</td>
<td>2.9 (0.2-7)</td>
<td>3.4 (0.1-10.8)</td>
<td>0.8 (0.5-1.7)</td>
<td>0.4 (0.1-1)</td>
<td>1.0 (0.2-8)</td>
<td>2.4 (0.4-6)</td>
<td>3.8 (0.9-9)</td>
</tr>
<tr>
<td>No. of exacerbations</td>
<td>2</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-5 (pg/mL)</td>
<td>8 (2-14)</td>
<td>12 (0-65)</td>
<td>7 (0-24)</td>
<td>5 (0-10)</td>
<td>Not collected at this visit</td>
<td>Not collected at this visit</td>
<td>6 (0-18)</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>79 (60-101)</td>
<td>76 (59-98)</td>
<td>76 (49-102)</td>
<td>75 (47-99)</td>
<td>75 (52-99)</td>
<td>80 (47-111)</td>
<td>77 (47-98)</td>
</tr>
<tr>
<td>PEF</td>
<td>Not measured @ visit</td>
<td>410 (300-480)</td>
<td>432 (210-529)</td>
<td>404 (210-529)</td>
<td>413 (240-529)</td>
<td>421 (280-523)</td>
<td>443 (380-564)</td>
</tr>
<tr>
<td>ACQ score</td>
<td>1.74 (0-2.86)</td>
<td>1.57 (0-2.86)</td>
<td>1.22 (0.29-2)</td>
<td>1.02 (0-1.71)</td>
<td>1.36 (0-1.83)</td>
<td>1.65 (0-3.86)</td>
<td>1.14 (0.57-3.86)</td>
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<tr>
<td>FeNO</td>
<td>62.2 (15-153.4)</td>
<td>47.4 (11-141.7)</td>
<td>39.1 (9.3-101.1)</td>
<td>50.5 (9.7-163.7)</td>
<td>62.1 (20.5-98.6)</td>
<td>Not collected at this visit</td>
<td>49.9 (31.1-86)</td>
</tr>
<tr>
<td>BVAS score</td>
<td>10.5 (3-18)</td>
<td>6.9 (3-15)</td>
<td>6.1 (0-11)</td>
<td>6.4 (0-17)</td>
<td>7.4 (0-14)</td>
<td>9.3 (3-12)</td>
<td>8.0 (0-23)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>6.2 (0.6-15.8)</td>
<td>3.9 (0.8-10.5)</td>
<td>6.1 (0.9-17.1)</td>
<td>4.2 (0.8-19.3)</td>
<td>7.5 (0.8-27.4)</td>
<td>3.1 (0.8-12.4)</td>
<td>6.5 (0.4-19.6)</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>8 (2-25)</td>
<td>7 (2-20)</td>
<td>10 (3-21)</td>
<td>9 (2-25)</td>
<td>11 (1-26)</td>
<td>4 (1-6)</td>
<td>7 (2-27)</td>
</tr>
</tbody>
</table>

n=7

Kim et al, J Allergy Clin Immunol 2010;125:1336-43
Kahn et al, J Allergy Clin Immunol 2010;125:267-70
Moosig et al, Ann Intern Med 2011;155; 341-343
n=9, received 9 monthly IV infusions, then MTX
→ mean f/u 22 months = 6/9 relapsed (5 major in 3; 7 minor in 5)
CanVasc network and research on vasculitis
Objectives

- **Initiate, conduct, and promote studies on vasculitis across Canada** (from CanVasc, VCRC or other vasculitis research groups) using an efficient and rapidly mobilisable network.
Objectives

• Initiate, conduct, and promote studies on vasculitis across Canada
• Organize a dedicated health and research network across Canada for patients with vasculitis with identification of referral (multidisciplinary) centers.
The network

... created in November 2011
## CanVasc network

<table>
<thead>
<tr>
<th>Province</th>
<th>City</th>
<th>Principal core members</th>
<th>Associated core members</th>
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</thead>
<tbody>
<tr>
<td>Ontario</td>
<td>Toronto</td>
<td>Dr. Simon Carette; Dr. Susan Benseler (Peds)</td>
<td>Dr. Christian Pagnoux; Dr. Paul Fortin; Dr. Heather Reich</td>
</tr>
<tr>
<td></td>
<td>Hamilton</td>
<td>Dr. Nader Khalidi</td>
<td>Dr. Michael Walsh; Dr. Gerard P. Cox</td>
</tr>
<tr>
<td></td>
<td>Ottawa</td>
<td>Dr. Nataliya Milman</td>
<td>Dr. Douglas C. Smith</td>
</tr>
<tr>
<td></td>
<td>Kingston</td>
<td>Dr. Tanveer Towheed</td>
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<tr>
<td></td>
<td>London</td>
<td>Dr. Lillian Barra</td>
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<tr>
<td>Québec</td>
<td>Sherbrooke</td>
<td>Dr. Patrick Liang</td>
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<tr>
<td></td>
<td>Montréal</td>
<td>Dr. Michelle Goulet</td>
<td>Dr. Christian Pineau; Dr. Yves Troyanov</td>
</tr>
<tr>
<td></td>
<td>Québec</td>
<td>Dr. Judith Trudeau</td>
<td></td>
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<tr>
<td>Nova Scotia</td>
<td>Halifax</td>
<td>Dr. Christine Dipchand; Dr. Volodko Bakowsky</td>
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<tr>
<td>British</td>
<td>Vancouver</td>
<td>Dr. Kam Shoja; Dr. David Cabral (Peds)</td>
<td>Dr. John Esdale; Dr. Kim Morishita (Peds); Dr. Ada Man</td>
</tr>
<tr>
<td>Columbia</td>
<td>Victoria</td>
<td>TBI</td>
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<tr>
<td>Alberta</td>
<td>Edmonton</td>
<td>Dr. Elaine Yacyshyn</td>
<td>Dr. Joanne Homik; Dr. Allan Murray (nephr.)</td>
</tr>
<tr>
<td></td>
<td>Calgary</td>
<td>Dr Aurel Fifi-Mah</td>
<td>Dr Diane Mosher</td>
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<tr>
<td>Manitoba</td>
<td>Winnipeg</td>
<td>Dr. David Robinson</td>
<td>Dr. Navjot Dhindsa</td>
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<tr>
<td>Saskatchewan</td>
<td>Saskatoon</td>
<td>Dr. Regina Taylor-Gjevre</td>
<td>Dr. Bindu Nair</td>
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<tr>
<td>Newfoundland</td>
<td>Saint Johns</td>
<td>Dr. Majed Khaibi</td>
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Objectives

• Initiate, conduct, and promote studies on vasculitis across Canada
• Organize a dedicated health and research network across Canada
• Develop educational and awareness programs for health care providers (training sessions, fellowship, annual meeting…).
CanVasc website

http://www.canvasc.ca

Creator and webmaster: Dr. Christian Pagnoux
Educational and awareness program

• REVISIT program (Canadian program)
  – For CME in ANCA vasculitis
  – Educational slide set (>150) and material
  – Presentation by core members (Montreal, Quebec, Yorkville, London, Vancouver, Kingston)

• CanVasc annual scientific meeting
  – 10 June 2011, Toronto - 80 attendees
  – Next one on Nov. 22nd, 2012 (Montréal)
2nd annual CanVasc meeting

Montréal, QC
November 22nd, 2012

Registration and information on
http://www.canvasc.ca
Objectives

• Initiate, conduct, and promote studies on vasculitis across Canada
• Organize a dedicated health and research network across Canada
• Develop educational and awareness programs for health care providers
• Establish and regularly update Canadian consensus for the diagnostic and therapeutic management of patients with vasculitis.
Canadian consensus for the management of ANCA vasculitides

- **Needs assessment questionnaire**
- Review of literature on the ~30 identified points
- Writing of draft with grading of evidence
- Reviewing by CanVasc core members

- Revised draft → subgroups (CSN, CRA, CSN committees)

- Revised draft V2 → Final version
Acknowledgments

Loïc Guillevin

All CanVasc members
Simon Carette
Nader Khalidi
Gery Cox
Kam Shojania…

All FVSG members
Luc Mouthon
Alfred Mahr…

Parameswaran Nair

All VCRC members
Simon Carette
Nader Khalidi
Peter Merkel…

CSS/EGPA association
Jane Dion
April 14 - 17 2013

"Institut des Cordeliers"
Paris - France

16th INTERNATIONAL
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