Third Annual CanVasc Scientific Meeting

Toronto, Ontario – October 24th, 2014
(Eaton Chelsea, Toronto)
9h00-16h30
Organizing Committee

- Dr. Christian Pagnoux,
- Dr. Simon Carette
- Dr. Nader Khalidi
Learning Outcomes

1. To understand the pathology, pathophysiology of the inflammatory response, and epidemiology of vasculitis as it relates to the size of the vessels involved.

2. To review the spectrum of vasculitis.

3. To learn about the various therapeutic options in treating patients with vasculitis.

4. To discuss issues pertinent to various specialties (internal medicine, rheumatology, nephrology and respirology) including collaboration on research activities and ongoing trials in Canada.
## Meeting Program

### Part 1 – Moderation, Dr. S. Carette

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>9h00-9h05</td>
<td>CanVasc recommendations for the management of ANCA-associated vasculitis &amp; General update on the management of ANCA-associated vasculitides</td>
<td>Dr. C. Pagnoux</td>
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<tr>
<td>9h30-10h00</td>
<td>Update on large vessel vasculitides (LVV)</td>
<td>Dr. N. Khalidi and Dr. N. Milman</td>
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<tr>
<td>10h00-10h30</td>
<td>Update on genetic studies in vasculitis</td>
<td>Dr. K. Siminovitch</td>
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<tr>
<td>10h30-10h45</td>
<td>Break</td>
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### Part 2 – Moderation, Dr. C. Pagnoux

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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>10h45-11h45</td>
<td>Treatment of vasculitis</td>
<td>Guest Speaker: DR. CAROL LANGFORD (Cleveland Vasculitis Clinic)</td>
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<tr>
<td>11h45-13h00</td>
<td>Lunch</td>
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### Part 3 – Moderation, Dr. N. Khalidi

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<tbody>
<tr>
<td>13h00-13h05</td>
<td>CanVasc (Website and educational activities)</td>
<td>Dr. C. Pagnoux</td>
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<tr>
<td>13h05-13h20</td>
<td>Vasculitis Foundation Canada (Patient support group)</td>
<td>Mr. J. Stewart</td>
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<tr>
<td>13h20-14h45</td>
<td>Ongoing activities and studies on vasculitis in Canadian CanVasc centers</td>
<td>All CanVasc core members</td>
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<td>14h45-15h00</td>
<td>Break</td>
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<tr>
<td>15h00-16h25</td>
<td>Ongoing enrolment for studies in Canada</td>
<td>Drs C. Pagnoux, M. Walsh, N. Khalidi, S. Carette</td>
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<tr>
<td>16h25-16h30</td>
<td>Conclusion</td>
<td>Dr. C. Pagnoux</td>
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CanVasc recommendations for the management of ANCA-associated vasculitis

Dr. C. Pagnoux
Disclosures

• Consulting and speaker fees
  – Hoffmann-La Roche
  – BMS

• Advisory boards
  – Hoffmann-La Roche
  – GSK

• Educational subventions (CanVasc)
  – Hoffmann-La Roche
  – Terumo BCT
  – Abbott Immunology
  – BMS
  – Pfizer-Amgen
  – Janssen-Cilag
  – Euroimmun
2012 Chapel hill Nomenclature

Genetically Distinct Subsets within ANCA-Associated Vasculitis


Association of Granulomatosis With Polyangiitis (Wegener’s) With HLA–DPB1*04 and SEMA6A Gene Variants

Evidence From Genome-Wide Analysis

Gang Xie,1 Delnaz Roshandel,1 Richard Sherva,2 Paul A. Monach,3 Emily Yue Lu,3 Tabitha Kung,1 Keisha Carrington,1 Steven S. Zhang,1 Sara L. Puit,4 Stephan Ripke,5 Simon Carette,1 Paul F. Dollarapa,6 Jeffrey C. Edberg, Gary S. Hoffman,8 Nader Khalidi,8 Carol A. Langford,8 Alfred D. Mahr,10 E. William St.Claire,11 Philip Sco,13 Ulrich Specks,13 Robert F. Spiera,1 John H. Stone,3 Steven R. Ytterberg,13 Soumya Raychaudhuri,5 Paul I. W. de Bakker,4 Lindsay A. Farrer,5 Christopher I. Amos,16 Peter A. Merkel,17 and Katherine A. Siminovitch18

Arthritis & Rheumatism 2013; 65 (9):2457–2468
76 in the **rituximab** group who had a CR
24 (32%) relapsed before M18

70 in the **CYC** had a CR
20 (29%) relapsed before M18

(P=0.16)
Objectives

• Review how CanVasc developed the recommendations
• Review the most important CanVasc recommendations for the management of ANCA vasculitis
• Understand the indications of the main drugs and biologics in the treatment of ANCA vasculitis
CanVasc founded in November 2010

**CanVasc Objectives**

The CanVasc group was officially created the 1st November 2010, in Toronto.

The proposed CanVasc objectives are to:

1. **organize a dedicated health and research network** with identification of referral (multidisciplinary) centers across Canada for patients with vasculitis. Establishment and regular updates of Recommendations for the diagnostic and therapeutic management of patients is part of this objective.
2. **initiate, conduct, and promote studies** (from CanVasc, VCRC or other vasculitis research groups) on vasculitides across Canada (epidemiological, observational, fundamental and, ultimately, therapeutic studies), using an efficient, established and rapidly mobilisable network.
3. **develop educational and awareness programs for health care providers** (training sessions, fellowship, annual meeting…).
4. **stand as the Canadian referral group to identify needs in vasculitis** and consider new drug approvals for vasculitis in Canada (advisory group).
Process

• Establishment and regular updates of **recommendations for the diagnostic and therapeutic management** of patients with ANCA-associated vasculitis

• **Needs assessment questionnaire**
  – CRA members
  – CanVasc member list
  – CTS (respirology) + CSN (nephrology)
  – including pediatricians, and some GIM
Process

→ 37 identified questions

• Review of literature on these questions
  – existing recommendations
  – PubMed + grey literature + proceedings since 2008

• Writing of draft 1 with grading of evidence
Process

- Revised draft (2) → 07/2014

- Revised draft (2)
  → CanVasc core members
  + subgroups (CTS, CSN, CRA members)

  → Patient association (VF Canada)
  → Nurses
What we want or would like

The available evidence
These are **NOT** guidelines!

– but the final document satisfies most of the AGREE II items and domains
Dissemination plan & the future

- CanVasc 2014 conference
- Canadian journal – short version
- Printed hand-outs – short and long versions
- CanVasc website (http://www.canvasc.ca)
- Various presentations
- Education material

- Updates
- Evaluation of its use and impact in practice
Drs. Lucy McGeoch (adult rheumatology), Marinka Twilt (pediatric rheumatology)

**CanVasc core members/Co-authors/Principal reviewers of all drafts:**

**CanVasc associated members/Co-authors/Principal reviewers of all drafts:**
Drs. Gerald P. Cox, Christine Dipchand, Heather Reich, Michael Walsh

**Additional reviewers for Draft 2:**
Drs. Maria Bagovich, Claire Barber, Joanne Bargman, Ken Bloka, Gilles Boire, Boussier, Robert Ferrari, Michele Hladunewich, Susan Huang, Jacob Karsch, Kim Legaut, Emil Nashi, Nathalie Roy, Evelyn Sutton, Yves Troyanov, Pearce G. Wilcox

**VF Canada:** John Stewart, Katherine Smith, Barbara Tuntoglu (board)

**Sandra Messier**
Funding source
Update on large vessel vasculitides (LVV)

Dr. N. Khalidi
Dr. N. Milman
Large Vessel Vasculitis Year in Review

Nader A. Khalidi, MD, FRCPC
Associate Professor

CanVasc 2014 Toronto
Disclosures

Abbott
Wyeth Amgen
BMS
Schering Plough
Roche Pharmaceuticals
Objectives

1. Update Imaging in GCA LVV

2. Update Treatment options in LVV

3. Update Relapse rates in LVV
Giant Cell Arteritis: Diagnostic Accuracy of MR Imaging of Superficial Cranial Arteries in Initial Diagnosis-Results from a Multicenter Trial

• 185 patients suspected of having GCA were included in a prospective three–university medical center trial

• GCA was diagnosed or excluded clinically in all patients (reference standard [final clinical diagnosis])

• In 53.0% of patients (98 of 185), temporal artery biopsy (TAB) was performed (diagnostic standard [TAB]).

Giant Cell Arteritis: Diagnostic Accuracy of MR Imaging of Superficial Cranial Arteries in Initial Diagnosis-Results from a Multicenter Trial

Giant Cell Arteritis: Diagnostic Accuracy of MR Imaging of Superficial Cranial Arteries in Initial Diagnosis-Results from a Multicenter Trial

Giant Cell Arteritis: Diagnostic Accuracy of MR Imaging of Superficial Cranial Arteries in Initial Diagnosis-Results from a Multicenter Trial

• Sensitivity of MR imaging was 78.4% and specificity was 90.4% for the total study cohort.

• Sensitivity was 88.7% and specificity was 75.0% for the TAB subcohort (first observer).

• Diagnostic accuracy was comparable for both observers, with good interobserver agreement (TAB subcohort, $\kappa = 0.718$; total study cohort, $\kappa = 0.676$).

Giant Cell Arteritis: Diagnostic Accuracy of MR Imaging of Superficial Cranial Arteries in Initial Diagnosis-Results from a Multicenter Trial

• Diagnostic accuracy of MR imaging was high in patients without and with sCS therapy for 5 days or fewer (area under the curve, ≥0.9) and was decreased in patients receiving sCS therapy for 6–14 days.

MRI for TA in GCA

191 patients were screened and 171 were included in our study.

MRI showed abnormal scalp arteries in 60 patients (35.1%) while biopsy was positive in 31 (18.1%).

MRI was positive in 29 of those 31 patients with positive TAB (Sensitivity 93.6%).

Rhéaume et al, Giant Cell Arteritis and MRI Evaluation of the cranial arteries 2014 ACR Accepted as oral presentation
Positron emission tomography assessment of large vessel inflammation in patients with newly diagnosed, biopsy-proven giant cell arteritis: a prospective, case–control study

• 32 consecutive, biopsy-proven, GCA patients treated with glucocorticoids for ≤3 days were included.

• The control group consisted of 20 individuals, who underwent PET/CT for cancer staging.

• Mean Standardized Uptake Value (SUV) was significantly higher in patients than in controls in all vessels explored and correlated with acute-phase reactants and serum IL-6.

• Yielded a sensitivity of 80% and a specificity of 79% for GCA diagnosis.

Positron emission tomography assessment of large vessel inflammation in patients with newly diagnosed, biopsy-proven giant cell arteritis: a prospective, case–control study

• A limitation of PET as a diagnostic tool is the lack of a standardised definition of vascular inflammation based on the intensity of 18fluorodeoxyglucose (FDG) uptake.

• Visual assessment of intensively positive cases may be clear, there is no consensus about the minimal intensity of FDG uptake necessary to define vascular inflammation

• Atherosclerosis and ageing may increase vascular FDG uptake, potentially leading to vasculitis overdiagnosis.

Leflunomide in GCA and PMR

- Patients with difficult-to-treat GCA and PMR retrospectively identified in the period from 2010 to 2013.

- The doses of corticosteroids and CRP values were noted before, after three months, and at the end of the treatment with leflunomide
Leflunomide in GCA and PMR: Results

• 23 patients were identified (12 with PMR and 11 with GCA).
• In PMR patients
  - reduction of 6mg/dL (CI 95% –10.9–34.2, \( P = 0.05 \)) in CRP and 3.7mg (CI 95% 0.5–7.0, \( P = 0.03 \)) in prednisolone dose was observed

• In GCA patients
  - reduction was 12.4mg/dL (CI 95% 0.7–25.5, \( P = 0.06 \)) in CRP and 6.6mg (CI 95% 2.8–10.3, \( P < 0.01 \)) in prednisolone dose
Angiotensin II Receptor Blockers in GCA

• Is concomitant treatment with angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) associated with changes in the outcome of patients with giant cell arteritis (GCA)?

M.A. Alba et al. Seminars in Arthritis and Rheumatism 43(2014)772–777
Angiotensin II Receptor Blockers in GCA

• Cohort of 106 patients with biopsy proven GCA

• Longitudinally followed up for close to 8 years

• Patients were stratified according to their treatment with ACEI, ARB, or no ACEI/ARB.

M.A. Alba et al Seminars in Arthritis and Rheumatism 43 (2014) 772–777
Angiotensin II Receptor Blockers in GCA

• Time to first relapse

• Number of flares

• Time to achieve a stable prednisone dose of < 10mg/day and <5 mg/day with no relapses

• Time required to completely discontinue prednisone

• Cumulative dose of prednisone received during the first year

M.A. Alba et al Seminars in Arthritis and Rheumatism 43 (2014) 772–777
Angiotensin II Receptor Blockers in GCA

• Patients receiving ARB presented a significantly longer relapse-free survival than patients treated with ACEI or patients not receiving ACEI/ARB (p = 0.02).

• The adjusted hazard ratio for relapses in patients treated with ARB was 0.32 (95% CI: 0.12–0.81, p = 0.017).

• Patients who received ARB achieved a prednisone maintenance dose of <10mg/day faster than all other patients (p = 0.0002).

M.A. Alba et al Seminars in Arthritis and Rheumatism 43(2014)772–777
Angiotensin II Receptor Blockers in GCA

• Conclusions: Addition of ARB to glucocorticoids is associated with lower relapse rate and more prolonged disease-free survival in patients with GCA.

M.A. Alba et al Seminars in Arthritis and Rheumatism 43(2014)772–777
Relapses in GCA

• This group also looked at prevalence, timing, and characteristics of relapses in patients with GCA

• Analyzed whether a relapsing course is associated with disease-related complications, increased glucocorticoid (GC) doses, and GC-related adverse effects.
Relapses in GCA

• Relapses were defined as reappearance of disease-related symptoms requiring treatment adjustment.

• Relapses were classified into 4 categories:
  - Polymyalgia rheumatica (PMR)
  - Cranial symptoms (including ischemic complications)
  - Systemic disease
  - Symptomatic large vessel involvement (Extremity claudication).
Relapses in GCA: Results

• 68 patients (64%) experienced at least 1 relapse, and 38 (36%) experienced 2 or more.

• First relapse
  - PMR in 51%
  - Cranial symptoms in 31%,
  - Systemic complaints in 18%
  - Symptomatic LVV 0%
Relapses in GCA: Results

- Relapses appeared predominantly, but not exclusively, within the first 2 years of treatment

- Only 1 patient developed visual loss

- Osteoporosis was more common in patients with relapses compared to those without (65% vs 32%, p=0.001).

- Cumulated prednisone dose during the first year was significantly higher in relapsing patients (6.21 vs 5.40g, p=0.015).

M.A. Alba et al Medicine • Volume 93, Number 5, July 2014
Tocilizumab in LVV

• 16 patients (14 women/2 men) with refractory aortitis diagnosed by imaging (CT angiography, MR angiography, and/or PET) were treated with TCZ.

• The underlying conditions were: Takayasu arteritis (TAK) (n=7 cases), giant cell arteritis (GCA) (n=7), relapsing polychondritis (RP) (n=1), and aortitis associated with retroperitoneal fibrosis (n=1).

Tocilizumab in LVV

• In all patient with GCA and in the patient with aortitis associated with retroperitoneal fibrosis TCZ was the first biologic drug used but in only 2 of 7 TAK patients.

• In the remaining cases anti-TNF inhibitors were prescribed before TCZ (standard dose was 8 mg/kg/iv/4 weeks).

Tocilizumab in LVV

- After a mean±SD follow-up of 11.8±6.6 months most patients experienced clinical improvement, showing reduction of erythrocyte sedimentation rate from 43±36 mm/1st h to 5±4 mm/1st h at last visit.

- At TCZ onset, 25% of patients had fever and 19% polymyalgia rheumatica

- These manifestations disappeared after 3 months of TCZ therapy.

- A corticosteroid sparing effect was also achieved (from 27.3±17.6 mg/day of prednisone at TCZ onset to 4.2±3.8 mg/day at last visit).

- TCZ had to be discontinued in a patient because of severe neutropenia.

Conclusions

• MRI has a high NPV and if negative, one can opt not to do a TAB

• PET/CT scan can be used diagnostically to show GCA LVV but not for temporal artery

• Leflunomide looks promising in LVV

• Actemra deserves further study in LVV and is being studied currently for GCA in GiACTA

• ARB’s are a fascinating adjunct that should probably be used more to help reduce amount of steroids in LVV
Update on genetic studies in vasculitis

Dr. K. Siminovitch
Third CanVasc Scientific Meeting

Toronto, Ontario – October 24th, 2014
(Eaton Chelsea, Toronto)
9h00-16h30

Organizing Committee: Dr. Christian Pagnoux, Dr. Simon Carette and Dr. Nader Khalidi

Break

10h30-10h45
Treatment of vasculitis

Special Guest Speaker: Dr. Carol Langford
(Cleveland Vasculitis Clinic)
Third CanVasc Scientific Meeting

Toronto, Ontario – October 24th, 2014
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Organizing Committee: Dr. Christian Pagnoux, Dr. Simon Carette and Dr. Nader Khalidi

Lunch

11h45-13h00
CanVasc
(Website and educational activities)

Dr. C. Pagnoux
Website: http://www.canvasc.ca

- List of members / centers
- Vasculitis reviews
- Meeting information
- Study information

- Forum for members
- Dropbox for core members
Explore CanVasc and its affiliated centers across Canada

CanVasc is the Canadian network for research on vasculitides. It was created in November 2010 by Drs. Pagnoux, Carette and Khalidi. The first task was to identify referral medical centers and physicians across Canada with expertise in vasculitis and who were willing to be part of this new research group (core members). Among its several other aims, important ones are to help conduct studies on vasculitis, provide support and educational material on vasculitides for physicians and other health care professionals and, eventually, optimize the therapeutic management of patients with these rare diseases.

CLICK HERE for more information on CanVasc.
CLICK HERE for more information on national CanVasc meetings

CanVasc FORUM (and link to CanVasc DropBox) can be Accessed from Here
(for CanVasc registered physicians only)

COMING SOON: The next national CanVasc MEETING will be held on October 24, 2014 in TORONTO!

This will be the 3rd national CanVasc scientific conference, open to all health care professionals. Several lectures to update your knowledge and awareness of ongoing research on vasculitides will be given, including by international guest speakers and CanVasc members from all across Canada. The pre-program and other information on this conference can be downloaded by clicking Here

Register now by clicking here (free registration for CanVasc members and fellows)!

On the following day, the Vasculitis Foundation Canada (patient support association) will hold its annual meeting as well. More information here.

Review studies on vasculitis actively recruiting in Canada

Several prospective studies on vasculitides are ongoing across the world, including in several Canadian centers. Have a brief overview of these latter ones, including PEXIVAS, DOVAS, BREVAS, RITAZAREM, MIRRA, TAPIR and GIACATA on the study webpage and determine whether any of your patients could participate to one of them.

Update your knowledge on vasculitis with CanVasc online materials

- READ the latest CanVasc reviews of recent articles: commented summaries of selected and important articles on vasculitis, for physicians to keep up the pace with scientific publications on vasculitis on the Vasculitis page!
  - Low dose rituximab for remission induction in ANCA-associated vasculitides. October 2014
  - The new histopathologic classification of ANCA-Associated GN and its association with renal outcomes in childhood. September 2014
  - ADA2 mutations in polyarteritis nodosa and early-onset stroke, March 2014
  - Abatacept for relapsing limited GPA, December 2013
  - 2013 ACR selected abstract review, November 2013 (bottom of meeting page)

- Download some presentations given by CanVasc members at conferences and meetings; go to the Meeting page!

Become a CanVasc member

If you are a health care provider interested in vasculitis and CanVasc activities, you can register by simply sending us an email (admin@canvasc.ca) specifying your name, surname, profession, address and full affiliations. At this time, membership is free and does not imply anything (please note that core, associated and affiliated member status is for physicians already identified by the CanVasc bureau).

You can receive occasional information by email on the CanVasc meetings or studies. CanVasc is a non-profit scientific network. You
# CanVasc core members

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<th>City</th>
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<th>Associated members</th>
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<tr>
<td>Ontario</td>
<td>Toronto</td>
<td>Dr. Simon Carette; Dr. Rae Yeung (Peds)</td>
<td>Dr. Christian Pagnoux; Dr. Heather Reich</td>
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<td></td>
<td>Hamilton</td>
<td>Dr. Nader Khalidi</td>
<td>Dr. Michael Walsh; Dr. Gerard P. Cox; Dr. Parameswaran Nair</td>
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<td>Ottawa</td>
<td>Dr. Nataliya Milman</td>
<td>Dr. Douglas C. Smith; Dr. Shaun Kitty (ENT); Dr. Brendon McCormick (Nephr.); Dr. Peter Magner (Nephr.); Dr. Nav Voduc (Respi.); Dr. Shawn Aaron (Respi.)</td>
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<td>Kingston</td>
<td>Dr. Tanveer Towheed</td>
<td>Dr. Michel Melanson (Neuro.); Dr. Marie Clements-Baker</td>
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<td>London</td>
<td>Dr. Lillian Barra</td>
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<td>Cambridge</td>
<td>Dr. Leilani Famorca</td>
<td>Dr. Brian Hanna</td>
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<td>Newmarket</td>
<td>Dr. Carter Thorne</td>
<td>Dr. Nooshin Samadi</td>
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<td>Québec</td>
<td>Sherbrooke</td>
<td>Dr. Patrick Liang</td>
<td>Dr. Ariel Masetto; Dr. Guylaine Arsenault</td>
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<td>Montréal</td>
<td>Dr. Michelle Goulet; Dr. Christian Pineau</td>
<td>Dr. Yves Troyanov; Dr. Evelyne Vinet; Dr. Eric Rich; Dr. Sonia Brachemi</td>
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<td>Dr. Judith Trudeau; Dr. Paul Fortin</td>
<td>Dr. David Philibert (Nephr.)</td>
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<td>Halifax</td>
<td>Dr. Volodko Bakowsky; Dr. Christine Dipchand</td>
<td>Dr Colm McParland (Resp.)</td>
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<td>British Columbia</td>
<td>Vancouver</td>
<td>Dr. Kam Shojania; Dr. David Cabral (Peds)</td>
<td>Dr. John Esdaile; Dr. Kim Morishita (Peds); Dr. Ada Man; Dr. Barry Kassen</td>
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<tr>
<td>Alberta</td>
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<td>Dr. Elaine Yacyshyn</td>
<td>Dr. Joanne Homik; Dr. Allan Murray (Nephr.)</td>
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<td></td>
<td>Calgary</td>
<td>Dr Aurore Fifi-Mah</td>
<td>Dr Diane Mosher; Dr. Charlene Fell (Resp.)</td>
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<td>Manitoba</td>
<td>Winnipeg</td>
<td>Dr. Navjot Dhinda</td>
<td>Dr. David Robinson</td>
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<td>Saskatchewan</td>
<td>Saskatoon</td>
<td>Dr. Regina Taylor-Gjevre</td>
<td>Dr. Bindu Nair; Dr. Jim Barton (Nephr.); Dr. Julian Midgley (Nephr. Peds)</td>
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<tr>
<td>Newfoundland</td>
<td>Saint John's</td>
<td>Dr. Majed Khaishi</td>
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Lower doses of rituximab for remission induction in ANCA-associated vasculitides?

Two studies on the use of lower doses of rituximab for induction in ANCA-associated vasculitides have just been published. The first retrospective one (Moog et al.) evaluated the efficacy of a single dose of rituximab (375 mg/m2) for remission induction and maintenance in (ANCA)-associated vasculitis in 16 patients. Patients were followed over a period of 24 months. They could be re-treated for maintenance with a single dose (every 6 to 9 months) in case of rising antibody titres or B-cell return. Remission (absence of disease activity during the past 3 months with a prednisolone dose of less than 7.5 mg) was achieved in 11 patients (68.8%), with a median time to remission of 6.4 months. During the follow-up period, 9 patients had a relapse, with a mean time to relapse of 5.3 months (4 to 24 months). At 24 months, 9 of these 11 initial responders (82%) were in remission, including 2 who had experienced a relapse during their follow-up. Importantly, all patients also continued corticosteroid and/or DMARD (AZA, MMF or LEF) for all but 4 of the 16 patients therapy over the study follow-up.

The second pseudo-prospective study (Tuner-Stokes et al.) included 19 patients with ANCA-associated vasculitides. Induction rituximab also included one single infusion of 375mg per m2. Eight (42%) were on additional immunosuppression at the time of rituximab treatment. Complete remission (defined here as the absence of clinical features of vasculitis for 3 months with a prednisolone dose of less than 10 mg/day) was achieved in 80% of patients at 3 months. There was no difference in the probability of achieving remission between anti-MPO- and anti-PR3-positive patients. Four patients (21%) had a disease relapse. Median time to B cell repopulation was 9.2 months and to disease relapse/redose was 27 months.

Both articles questioned the approved rituximab dosing (375 mg per m2 x 4) to achieve remission in active ANCA-associated vasculitides. Using one single dose seems to achieve remission in an important percentage of patients, but clearly not all. It is difficult to directly compare the results of these two studies to those of the RAVE trial, because of major differences in their study designs, the small number of patients studied here, and the different definitions used to define remission. Moreover, the use of concomitant immunosuppressors complicates the interpretation of the results of these two studies. However, the possibility to use lower doses of rituximab, which remains an expensive drug not superior to the cyclophosphamide-azathioprine regimen according to the RAVE and RITUXVAS trials, deserves further evaluation.


The new histopathologic classification of ANCA-Associated GN and its association with renal outcomes in childhood

In this study the proposed histopathologic classification for adult ANCA associated GN is validated in a retrospective, single center cohort of 40 children diagnosed with ANCA-GN. Renal biopsy specimens were reviewed and classified by a pathologist blinded for renal outcome. Children were followed for a mean of 2.4 years. Biopsy specimens showed the following classification: focal in 13, crescentic in 20, mixed in 2 and sclerotic 5 patients. The composite renal endpoint differed significantly among the biopsy groups. The probability of having a eGFR>60 ml/min per 1.73m2 at 2 years was 100% in the focal group, 56% in the crescentic group, and 0% for the sclerotic group.

This study shows the additional clinical utility of the proposed histopathologic classification system and its ability to clearly discriminate kidney outcomes among childhood ANCA GN patients as well as adults. In the future this could permit optimization of treatment strategies and ultimately lead to better evidence for the treatment of this severe disease in children. - M Twilt, 09 Sept 2014.


Adenosine Deaminase " (ADA 2) mutations in Polyarteritis Nodosa vasculopathy and early-onset stroke

Two studies report on ADA 2 mutations in the NEJM in February. The NIH group describes 9 patients with ADA 2 mutations (recessive mutations in CECL; joint and predominately large vessel vasculopathy, candidate 1). Patients presented with intermittent fevers, rash, and joint pain. Some had prominent small vessel vasculopathy (smoking or hypertension, candidate 2).
The 3rd and 2014 national scientific CanVasc meeting (there was none in 2013, as vasculitis physicians attended the ANCA workshop in Paris) will be held in Toronto, the 24 October 2014 (Delta Chelsea Eaton Hotel, downtown). The pre-program is available HERE.

REGISTER NOW BY CLICKING HERE (free for fellows and already registered CanVasc members)

- Core member meetings

  Last face-to-face core member business meeting was held during the 2014 Whistler CRA conference, on February 27th, 2014. Next face-to-face “working meeting” will take place on Thursday, October 23rd, 2014, from 4:30PM to 7PM, in the large conference room, Mount Sinai Hospital, i.e. the day before the 2014 annual meeting (this working meeting is open only to core members and/or their associates/delegates - more information will be sent by email directly to each core members prior to the meeting).

- Core member teleconferences

  The last core member teleconference was held on October 9, 2014. More information on the next one (around June2015) will be sent to each core members directly.

Forthcoming vasculitis meetings (or meetings with vasculitis sessions) and lectures

- 2014 ACR scientific conference, Boston, USA, November 13 - 19, 2014


- 2015 CRA’s annual meeting, Québeccity, QC, February 4 - 7, 2015

  Website http://rheum.ca.

- 2015 ACR scientific conference, San Francisco, USA, November 7-11, 2015


Downloadable vasculitis presentations (PowerPoint/pdf files)

Here are some of the presentations given by CanVasc members during past meetings (for most of them, modified and shortened, in order to respect confidentiality and not to disseminate unpublished results that have been presented orally at the meeting - feel free to contact us for more information).

First (2011) Annual CanVasc meeting

  - The meeting program
  - The French and EUVAS networks
Prognostic scores

- FFS 1996
- Revisited 2009 FFS

Activity scores

- BVAS version 2003 (active form sheet)
  - link to online BVAS calculator (only for new active manifestations)
  - BVAS v3 (active form sheet + scoring scale)
  - BVAS v3 (active and persistent form sheet)
  - BVAS v3 (active and persistent form sheet + scoring scale)

- BVAS/GPA (WG)
  - Formula for scoring BVAS/GPA (WG)

- BVAS version 1996 (original)
- PVAS (Pediatric score)
- ITAS 2010 (Takayasu arteritis)
  - ITAS 2010 glossary

Damage scores

- VDI
- PVDI (Pediatric score)

PACNS

- Barthel
- Modified Rankin score
- NIH stroke scale

Miscellaneous

- Ontario criteria for rituximab coverage (induction only) - March 2012
- British Columbia criteria for rituximab coverage/application
- Common Terminology Criteria for Adverse Events (NIH Sept. 2009 - 200 pages)
- Link to CanVasc member FORUM with link to CanVasc DropBOX
- TRAIN YOURSELVES FOR BVAS AND VDI scoring with R. Luqmani HERE!!
## Summary table of ongoing studies

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Study Name/Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active GCA</td>
<td>GiACTA (&lt;6 weeks)</td>
</tr>
<tr>
<td>Severe GPA/MPA with lung or kidney</td>
<td>PEXIVAS (&lt;2 weeks) - website</td>
</tr>
<tr>
<td>GPA/MPA entering remission</td>
<td>BREVAS (&lt;2 wks remission)</td>
</tr>
<tr>
<td>GPA on prednisone for maintenance</td>
<td>TAPIR (website)</td>
</tr>
<tr>
<td>Relapsing severe GPA/MPA</td>
<td>RITAZAREM (at relapse) - website</td>
</tr>
<tr>
<td>Refractory EGPA</td>
<td>MIRRA</td>
</tr>
<tr>
<td>All</td>
<td>VCRC cohort (any time)</td>
</tr>
<tr>
<td></td>
<td>VCRC contact registry (any time)</td>
</tr>
<tr>
<td></td>
<td>DCVAS (&lt;2 years)</td>
</tr>
<tr>
<td>PACNS</td>
<td>INTERSpace</td>
</tr>
</tbody>
</table>

To read more information on each study, click on the name on the study when a link is available and/or read below.

**SOON:** Other studies will start, including ABROGATE (abatacept for limited relapsing GPA) and CLASSIC (CCX68, anti-C5Ra, for systemic active GPA). Stay tuned!

**NOTE (27 February 2014):** The ABAVAS trial (randomized therapeutic study to evaluate the adjunction of abatacept (CTL4-Ig) to corticosteroids in patients with either giant cell arteritis or Takayasu’s arteritis) is no longer recruiting.

If you still need more detail on these studies or if you think that one of your patients could be eligible for any of this study, do not hesitate to contact us as well (admin@canvasc.ca).

---

**PEXIVAS**

PEXIVAS trial is a multicentre, international, phase III, open label randomised controlled therapeutic trial to investigate plasma exchange and glucocorticoid dosing in the treatment of ANCA-associated vasculitis. It is conducted under the aegis of the VCRC, EUVAS and NIH. Several centers in Canada are participating, including centers involved in CanVasc, like Hamilton, where Dr. M. Walsh (associated member of CanVasc), who originally worked on the trial design and is the main investigator for Canada, is established.

The first Canadian patient has been enrolled in late March 2011 in Hamilton, which was the first open center in Canada. All other Canadian centers (London, Edmonton, Vancouver, SMH-Toronto, MSH-Toronto, Calgary, UHN-TGH/TWH-Toronto, Montreal, Ottawa) are now interested in participating.'
For physicians

Canvasc MD member FORUM

Please note that ONLY medical doctors, registered as CanVasc members (first register to become CanVasc member then create a forum account - access to forum will then be granted). This is a secured and password-restricted forum.

Vasculitis Clinical Research Consortium (VCRC)

The Vasculitis Clinical Research Consortium is an integrated group of academic medical centers, patient support organizations, and clinical research resources dedicated to conducting clinical research in different forms of vasculitis. The website contain medical information for physicians, health care providers but also patients.

French Vasculitis Study Group (FVSG)

The FVSG (French Vasculitis Study Group) is a non-profit association created in 1981 by Prof. Loic Guillevin. The FVSG’s goals in the field of systemic vasculitides are to aid and promote research, diffuse updated information to doctors and patients, organize and coordinate therapeutic trials, and compile a register of doctors and investigators working in the field of vasculitis.

European vasculitis study group

European Vasculitis Study group (EUVAS) is the open collaborative research group of European physicians interested in research and education in vasculitis. The website provide some information on EUVAS activities.

The Johns Hopkin Vasculitis Center WebSite

The purpose of this Website is mainly to provide information about vasculitis for patients, including easy-to-print booklets on each of the main vasculitides, but physicians and research coordinators may also find a lot of useful information and practical tools.

Cleveland Clinic CME Website - Vasculitis

The Cleveland Clinic Center for Continuing Education has been committed to sharing a wealth of knowledge with physicians, nurses, and other medical professionals across the country and all over the world for more than 75 years. This website contains rich educational material and updates on vasculitis and vasculitis research.

RheumInfo.com

RheumInfo.com is website developed by Dr. Andy Thompson & Marlene Thompson (London, ON) to provide free, honest, accurate, and reliable information for patients and physicians dealing with rheumatic disease. Many simple easy-to-use booklets on treatment, which can be given to help patients manage their treatment on a daily basis, are downloadable.
<table>
<thead>
<tr>
<th>Section</th>
<th>Posts</th>
<th>Topics</th>
<th>Last Post</th>
</tr>
</thead>
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<tr>
<td><strong>Forum Information</strong></td>
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<tr>
<td><strong>CanVasc Activities and Information</strong></td>
<td>1</td>
<td>1</td>
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<td>Last post by arifine in RedCap use for database on 22 May 2014, 23:48:01</td>
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<td><strong>General Discussion on Vasculitis</strong></td>
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<td><strong>Difficult Cases</strong></td>
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<td>4</td>
<td>Last post by lbrata in Re: Hypocomplementemets U... on 19 July 2014, 18:11:38</td>
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<td><strong>CanVasc Consensus and Recommendations</strong></td>
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<td>Month</td>
<td>Unique visitors</td>
<td>Number of visits</td>
<td>Pages</td>
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<td>Jan 2014</td>
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<td>2,319</td>
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<td>2,569</td>
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<td>Jul 2014</td>
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<td>Aug 2014</td>
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<td>Sep 2014</td>
<td>1,127</td>
<td>1,972</td>
<td>4,574</td>
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<td><strong>Oct 2014</strong></td>
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<td><strong>1,007</strong></td>
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<td>Dec 2014</td>
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<td><strong>Total</strong></td>
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<td><strong>15,041</strong></td>
<td><strong>34,715</strong></td>
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<tr>
<td>Country / Territory</td>
<td>Sessions</td>
<td>% New Sessions</td>
<td>New Users</td>
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<tr>
<td>Canada</td>
<td>3,176</td>
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<tr>
<td>France</td>
<td>1,149</td>
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<td>947</td>
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<tr>
<td>United States</td>
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<tr>
<td>Brazil</td>
<td>468</td>
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<td>463</td>
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<td>Algeria</td>
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<tr>
<td>United Kingdom</td>
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<tr>
<td>India</td>
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<td>Belgium</td>
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<td>Morocco</td>
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### Regional Statistics

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<tr>
<th>Region</th>
<th>Sessions</th>
<th>% New Sessions</th>
<th>New Users</th>
<th>Bounce Rate</th>
<th>Pages / Session</th>
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<tr>
<td>Ontario</td>
<td>1,871</td>
<td>63.50%</td>
<td>1,188</td>
<td>55.10%</td>
<td>2.55</td>
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<tr>
<td>Quebec</td>
<td>651</td>
<td>71.27%</td>
<td>464</td>
<td>61.90%</td>
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<tr>
<td>Alberta</td>
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<td>73.07%</td>
<td>236</td>
<td>65.33%</td>
<td>1.85</td>
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<tr>
<td>British Columbia</td>
<td>214</td>
<td>64.95%</td>
<td>139</td>
<td>54.67%</td>
<td>2.42</td>
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<tr>
<td>Saskatchewan</td>
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<td>56.82%</td>
<td>25</td>
<td>31.82%</td>
<td>3.61</td>
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<tr>
<td>Manitoba</td>
<td>40</td>
<td>77.50%</td>
<td>31</td>
<td>52.50%</td>
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<tr>
<td>Nova Scotia</td>
<td>19</td>
<td>78.95%</td>
<td>15</td>
<td>36.84%</td>
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<tr>
<td>New Brunswick</td>
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<td>72.73%</td>
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<td>72.73%</td>
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<tr>
<td>Newfoundland and Labrador</td>
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<td>100.00%</td>
<td>3</td>
<td>100.00%</td>
<td>1.00</td>
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**Map:**
- Color scale: 3 to 1,871
- Regions shaded in varying intensities of blue, with a legend indicating the range of values.
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<thead>
<tr>
<th>OS</th>
<th>Hits</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Windows</td>
<td>96,493</td>
<td>69.2 %</td>
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<td>Macintosh</td>
<td>23,092</td>
<td>16.5 %</td>
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<td>Unknown</td>
<td>11,041</td>
<td>7.9 %</td>
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<tr>
<td>Linux</td>
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<td>3.9 %</td>
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<tr>
<td>Java</td>
<td>2,803</td>
<td>2 %</td>
</tr>
<tr>
<td>BSD</td>
<td>207</td>
<td>0.1 %</td>
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<tr>
<td>Unknown Unix system</td>
<td>134</td>
<td>0 %</td>
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<tr>
<td>BlackBerry</td>
<td>65</td>
<td>0 %</td>
</tr>
<tr>
<td>Symbian OS</td>
<td>5</td>
<td>0 %</td>
</tr>
<tr>
<td>iOS (iPhone/iPod/iPad/...)</td>
<td>4</td>
<td>0 %</td>
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<tr>
<td>Others</td>
<td>8</td>
<td>0 %</td>
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</table>

<table>
<thead>
<tr>
<th>Grabber</th>
<th>Hits</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS Internet Explorer</td>
<td>33,868</td>
<td>24.3 %</td>
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<tr>
<td>Mozilla</td>
<td>31,102</td>
<td>22.3 %</td>
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<tr>
<td>Google Chrome</td>
<td>24,332</td>
<td>17.4 %</td>
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<tr>
<td>Firefox</td>
<td>21,353</td>
<td>15.3 %</td>
</tr>
<tr>
<td>Safari</td>
<td>19,167</td>
<td>13.7 %</td>
</tr>
<tr>
<td>Unknown</td>
<td>5,169</td>
<td>3.7 %</td>
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<tr>
<td>Opera</td>
<td>1,264</td>
<td>0.9 %</td>
</tr>
<tr>
<td>Netscape</td>
<td>1,106</td>
<td>0.7 %</td>
</tr>
<tr>
<td>Android browser (PDA/Phone)</td>
<td>1,045</td>
<td>0.7 %</td>
</tr>
<tr>
<td>Samsung (PDA/Phone browser)</td>
<td>571</td>
<td>0.4 %</td>
</tr>
<tr>
<td>Others</td>
<td>372</td>
<td>0.2 %</td>
</tr>
</tbody>
</table>
We are now on (right?) track
Vasculitis Foundation Canada
(Patient support group)

Mr. J. Stewart
Ongoing activities and studies on vasculitis in Canadian CanVasc centers

All CanVasc core members
The CanVasc core members centers
# Executive Committee

(to be elected every 4 years, as of June 2014)

**President:** Dr. Simon Carette  
**Vice-president:** Dr. Christian Pagnoux  
**Secretary:** Dr. Nader Khalidi

## Core Members

<table>
<thead>
<tr>
<th>Province</th>
<th>City</th>
<th>Principal Core Member (Level 1)</th>
<th>Associated Core Members (Level 2)</th>
<th>Affiliated Core Members / Colleagues (Level 3)</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ontario</td>
<td></td>
<td>Dr. Simon Carette; Dr. Rae Yeung (Peds.)</td>
<td>Dr. Christian Pagnoux; Dr. Heather Reich (Neph.)</td>
<td>Dr. Laurence Rubin; Dr. Ian Witterick (ENT); Dr. Joanne Bargman (Neph.); Dr. Mary Bell</td>
<td>Division of Rheumatology, Mount Sinai Hospital and University Health Network, The Joseph and Wolf Lebovic Building 60 Murray Street, Ste 2-220 Toronto, Ontario M5T 3L9 Tel. 416-586-4800 Ext. 8549 or 5519 E-mail: <a href="mailto:VasculitisClinic@mssinai.on.ca">VasculitisClinic@mssinai.on.ca</a></td>
</tr>
<tr>
<td>Hamilton</td>
<td></td>
<td>Dr. Nader Khalidi</td>
<td>Dr. Michael Walsh (Neph.); Dr. Gerard P. Cox (Respi.); Dr. Parameswaran Nair (Respi.)</td>
<td></td>
<td>Division of Rheumatology St. Joseph’s Healthcare Hamilton 25 Charlton Suite 708, Hamilton, Ontario, L8N 4A6 Phone: 905-521-9034 Fax: 905-521-8099</td>
</tr>
<tr>
<td>Ottawa</td>
<td></td>
<td>Dr. Nataliya Milman</td>
<td>Dr. Douglas C. Smith</td>
<td>Dr. Shaun Kilty (ENT); Dr. Brendon McCormick (Neph.); Dr. Peter Magner (Neph.); Dr. Nav Voduc (Respi.); Dr. Shawn Aaron (Respi.); Dr. Kangisberg (Derm.); Dr. Marco Gomez (Lung Pathol.)</td>
<td>Arthritis Centre at the Ottawa Hospital, Riverside Campus 1967 Riverside Drive, box 37, K1H 7W9, Tel: 613-738-8400, ext. 81871 Fax: 613-738-8228</td>
</tr>
<tr>
<td>Kingston</td>
<td></td>
<td>Dr. Tanveer Towheed</td>
<td>Dr. Marie Clements-Baker; Dr. Michel Melanson (Neurol.)</td>
<td>Dr. Andre Tan (ENT); Dr. David Holland (Neph.); Dr. Christine D’Arsigny (Respi.)</td>
<td>Department of Medicine Queen’s University Room 2066, Etherington Hall, Kingston, Ontario, K7L 3N6 Phone: 613-533-6896</td>
</tr>
</tbody>
</table>
- Toronto + registries
- Hamilton
- Newmarket
- Kitchener
- Kingston
- London
- Ottawa
- Montreal
- Sherbrooke
- Quebec
- Winnipeg
- Saskatoon
- Edmonton
- Calgary
- Halifax
- St Johns
- Vancouver
Registries

• Different options, but the same structure and, eventually, items
  – Access
  – RedCap
  – BrainWorks
Current instrument: **Adult - Patient Entry**

**NOTE:** Please be aware that branching logic and calculated fields will not function on this page. They only work on the survey pages and data entry forms.

<table>
<thead>
<tr>
<th>Field</th>
<th>Options</th>
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<tbody>
<tr>
<td>Does the patient meet 1990 ACR and/or Chapel Hill Criteria?</td>
<td>Yes</td>
</tr>
<tr>
<td>Has the patient consented to study?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is the patient older than 18 years of age?</td>
<td>Yes</td>
</tr>
<tr>
<td>Year of birth</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
<td>Date of first symptoms attributable to vasculitis (other than asthma in EGPA)</td>
<td></td>
</tr>
<tr>
<td>Date of Diagnosis</td>
<td></td>
</tr>
<tr>
<td>PRIOR RELAPSES</td>
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<tr>
<td>Has the patient ever relapsed after having achieved a first remission prior to entry in the adult study?</td>
<td>No</td>
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<tr>
<td>If YES, precise the date(s) of all previous relapses</td>
<td></td>
</tr>
<tr>
<td>First relapse period: Onset date</td>
<td></td>
</tr>
<tr>
<td>First relapse period: End date</td>
<td></td>
</tr>
<tr>
<td>Second relapse period: Onset date</td>
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<tr>
<td>Second relapse period: End date</td>
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<tr>
<td>Third relapse period: Onset date</td>
<td></td>
</tr>
<tr>
<td>Third relapse period: End date</td>
<td></td>
</tr>
</tbody>
</table>
Adult Patient – Screens
Launching a patient’s visit
**Observe the Green Banner for an Adult Patient Visit**
Imaging > Posterior Circulation

- Normal circulation

R & L Posterior Cerebral Artery PCA divided in Segments P1-P3

Segment

R P3 PCA

L P3 PCA

R P2 PCA

L P2 PCA

R P1 PCA

L P1 PCA

R Superior Cerebellar Artery

L Superior Cerebellar Artery

R Posterior Communicans P-COMM

L Posterior Communicans P-COMM

R Anterior Inferior Cerebellar Artery AICA

L Anterior Inferior Cerebellar Artery AICA

Basilar Artery

R C1 Vertebral Artery

L C1 Vertebral Artery

R Subarachnoidal Vertebral Artery

L Subarachnoidal Vertebral Artery

R C2 Vertebral Artery

L C2 Vertebral Artery

R Cervical Vertebral Artery

L Cervical Vertebral Artery

R & L Vertebral Artery divided in Segments
Toronto

- Mount Sinai Hospital
- 3 days per week of vasculitis clinic (60 pts.)
- Combined CNS, nephrology and pediatric clinics
- Vasculitis fellows (and fellowship)
- Sub-PI / site for VCRC, DCVAS and pharma RCTs
- Currently involved in 7 RCTs (6 recruiting) + 2 that will open soon
- 1 research assistant, 1 REB (shared) assistant
Third CanVasc Scientific Meeting

Toronto, Ontario – October 24th, 2014
(Eaton Chelsea, Toronto)

9h00-16h30

Organizing Committee: Dr. Christian Pagnoux, Dr. Simon Carette and Dr. Nader Khalidi

Break

14h45-15h00
Other studies enrolling patients in

Drs. C. Pagnoux, N. Khalidi, M. Walsh, S. Carette
Toronto, 24 October 2014
<table>
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2012 revised Chapel Hill nomenclature

- **Immune Complex Small Vessel Vasculitis**
  - Cryoglobulinemic Vasculitis
  - IgA Vasculitis (Henoch-Schönlein)
  - Hypocomplementemic Urticarial Vasculitis (Anti-C1q Vasculitis)

- **Medium Vessel Vasculitis**
  - Polyarteritis Nodosa
  - Kawasaki Disease

- **Large Vessel Vasculitis**
  - Takayasu Arteritis
  - Giant Cell Arteritis

- **Anti-GBM Disease**

- **ANCA-Associated Small Vessel Vasculitis**
  - Microscopic Polyangiitis
  - Granulomatosis with Polyangiitis (Wegener’s)
  - Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)

*Jennette et al. Arthritis Rheum. 2013*
GiACTA – Giant Cell Arteritis and TCZ
A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF GEVOKIZUMAB IN THE TREATMENT OF GIANT CELL ARTERITIS

-XOMA 052 is a recombinant human-engineered monoclonal antibody that binds and neutralizes human IL-1b when administered every 4 weeks by s.c. injection.

-There are on-going trials in multiple inflammatory conditions.

-The rationale for IL-1 blockade as a therapeutic option in patients with GCA is as follows:
• IL1Ra KO mice develop large vessel vasculitis.
• In patients with GCA, IL1 is produced by the vessel wall infiltrate in a manner correlated with the intensity of the systemic inflammatory response and with corticosteroids requirements.
• IL-1 is also produced by the majority of activated circulating monocytes.
• IL-1 blocking therapy was shown to be effective in three patients with refractory GCA, yielding normalization of their inflammatory biomarkers and/or improvement in their symptoms.
A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF GEVOKIZUMAB IN THE TREATMENT OF GIANT CELL ARTERITIS

- Randomized, double-blind, multicentre, placebo-controlled trial, with 50, 25 patients in each arm with a total duration of 12 months.

- Previous GCA diagnosis according to the ACR 1990 criteria, (with at least one previous relapse).

- The diagnosis should be confirmed either by a temporal artery biopsy or (in case of negative or absent TAB), or a positive imaging with either FDG-PET scan or CT arteriogram.

- The patients should be on oral CS treatment between 5-30mg daily and have experienced a new GCA relapse limited to PMR-like or systemic symptoms.
A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF GEVOKIZUMAB IN THE TREATMENT OF GIANT CELL ARTERITIS
PEXIVAS

a RCT of plasma exchange and glucocorticoid dosing in ANCA associated vasculitis

On behalf of the PEXIVAS Trial Group
Complement Cascade and C5aR

- Complement cascade comprised by over 30 proteins
- Can be activated by three distinct pathways
- All pathways merge to form C3a, C5a, C3b and C5b-9
- Eculizumab (Soliris®) is an anti-C5 antibody
  - IV, expensive, risk of *Neisseria* infection (C5b-9 formation is blocked)
- CCX168 is a C5aR inhibitor
  - Oral, no risk of *Neisseria* infection
Alternative Complement Pathway in the Pathogenesis of Disease Mediated by Anti-Neutrophil Cytoplasmic Autoantibodies

C5a Receptor (CD88) Blockade Protects against MPO-ANCA GN

Hong Xiao,*† Daniel J. Dairaghi,‡ Jay P. Powers,‡ Linda S. Ertl,† Trageen Baumgart,‡ Yu Wang,† Lisa C. Seitz,‡ Mark E.T. Penfold,‡ Lin Gao,§ Peiqi Hu,*† Bao Lu,§ Norma P. Gerard,‖ Craig Gerard,‖ Thomas J. Schall,‡ Juan C. Jaen,‡ Ronald J. Falk,*† and J. Charles Jennette*†

*Department of Pathology and Laboratory Medicine and †UNC Kidney Center, University of North Carolina, Chapel Hill, North Carolina; ‡ChemoCentryx, Inc., Mountain View, California; §Department of Ophthalmology, University of Rochester, Rochester, New York; and ‖Department of Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts

Next step = a RCT in Europe and USA-Canada

Naïve or relapsing ANCA+ GPA/MPA/RLD, not too severe (1 “major” item, or ≥3 other items, or ≥2 renal items on the BVAS v.3; eGFR ≥ 20 mL per minute; no severe AH, Sat O2 >88%)

Up to approximately 45 subjects will be stratified 1:1:1

Group A: CCX168 10 mg BID for 12 weeks + IV CYC-AZA/ritux + CS

Group B: CCX168 30 mg BID for 12 weeks + IV CYC-AZA/ritux + CS

Group C: Placebo BID for 12 weeks + IV CYC/ritux + CS

End point at week 12 (with follow-up until week 24)
ChemoCentryx CL003_168 (CLASSIC Study)

• We are still looking for sites in Canada. If you are interested in participating, please contact:
  • Heather Lohr, Clinical Trial Manager at h.lohr@Medpace.com or 513-579-9911 ext. 2424
Human Genome Sciences and GSK
1. BE ≥18 YEARS OF AGE
2. HAVE A CLINICAL DIAGNOSIS OF GPA OR MPA
3. WITH EVIDENCE OF POSITIVE ANTI-PR3 OR ANTI-MPO ANCA AT SOME TIME DURING THE COURSE OF THE DISEASE
4. HAVING RECEIVED ONE OF FOLLOWING INDUCTION REGIMENS FOR THE MOST RECENT EPISODE OF ACTIVE DISEASE:
   A. RITUXIMAB (375MG/M²/WEEK X 4 OR 1G X 2) + HIGH DOSE CS
   B. CYCLOPHOSPHAMIDE (ORAL OR IV) + HIGH DOSE CS
5. BE IN CONFIRMED REMISSION (BVAS=0 ON 2 SUCCESSIVE VISITS SEPARATED BY AT LEAST 14 DAYS), 6 TO 26 WEEKS AFTER THE INITIATION OF INDUCTION THERAPY (AZA CAN HAVE BEEN STARTED ALREADY AT THE TIME OF REMISSION)

300-400 SUBJECTS WILL BE ENROLLED

A 1ST EFFICACY ANALYSIS WILL BE PERFORMED AFTER 66 SUBJECTS HAVE RELAPSED AND/OR AFTER ENROLMENT OF THE FIRST 300 PATIENTS
The Assessment of Prednisone In Remission Trial (TAPIR)

Key eligibility criteria include:

- Diagnosis of granulomatosis with polyangiitis (GPA)
- Required ≥ 20 mg/day of prednisone at some point in the last 12 months
- GPA currently in remission
- Currently taking between 6 mg and 20 mg of prednisone per day
- Age 18 or older

- Randomized to reduce prednisone dose to either 5 mg or 0 mg a day using standardized taper
- Subjects followed for 6 months
60 patients
Primary hypothesis is a difference of ≥30% in the relapse rate.
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<th>Cumulative</th>
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+ Patient-centric approach...
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Relapsing non-severe GPA within <28 days (modified ACR criteria):

a. No disease manifestations that would be scored as a major element in the BVAS/WG
b. Absence of any disease feature that poses an immediate threat to either a critical individual organ or the patient’s life

treatment failure rate through 12 months

150 patients
RITAZAREM

Rituximab (RTX) or azathioprine (AZA) for remission after RTX induction

- 190 GPA/MPA relapse
- Induction RTX 375mg/m²x4
- RTX group 1000mg / 4 months
- AZA group 2mg/kg/d

Induction 0-4 months
Remission treatment 4-24 months
Follow-up 24-48 months
MIRRA

- Relapsing or refractory EGPA, dx >6 months
- CS ≥7.5mg OD prednisone, stable for >4 weeks
  (± an immunosuppressant like AZA, MTX or MMF)
- With past Hx of relapse within past 2 years OR refractory
- Not too severely affected

- **Mepolizumab SQ 300mg, monthly until wk 48 vs. Placebo**
- Duration of clinical remission in weeks with BVAS=0 and CS≤4 mg/d

  - IºEP = 29% difference in the % of those in remission at W52 (80% placebo vs. 55% mepo; OR=3.5)
  - P 90%, alpha 5% → 70 pts per arm with HR = 0.5
Study design

Screening must occur between -1 and -4 weeks.

Oral corticosteroid dose stable from -4 weeks to Week 4.

Treatment period:
- MEPO 300 mg SC + standard of care (N=65) or
- PBO SC + standard of care (N=65)

13 study drug administrations

Follow-up period

Treatment period: Baseline to Week 52

Commence OCS tapering from Week 4.
### Active GCA
- **GiACTA (<6 wks CS)**

### GCA
- **Gevokizumab**

### Severe GPA/MPA with lung or kidney
- **PEXIVAS (<2 wks CS)**

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- **DCVAS (<2 years)**
VCRC patient registry

http://rarediseasesnetwork.epi.usf.edu/vcrc/index.htm

> 2,000
DCVAS Study

– ACR/EULAR diagnostic and classification criteria for vasculitis
– Number of centres: 118

This project anticipates to produce the following:

• 1) A new validated set of classification criteria for the primary systemic vasculitides.
• 2) A validated set of diagnostic criteria for the primary systemic vasculitides.
DCVAS Study

• How will the final revisions differ from the current ACR criteria?

• The main differences will be:

• Use modern diagnostic tests (e.g. ANCA, use of diagnostic ultrasound for GCA), new tools of disease activity (BVAS) and tools measuring vasculitis damage (VDI) to further refine the criteria.

• Develop a reference standard by using clustering of clinical features, from real and hypothetical cases so that an expert panel may define a boundary around these clinical features to define each disease

• Develop diagnostic criteria which can be used in daily clinical practice. The current ACR criterion was never intended for, and does not function well for this purpose.
DCVAS Study

Latest recruitment is over 3581 patients from 118 sites
Background: The Diagnostic and Classification Criteria for Vasculitis (DCVAS) Study is a multinational observational study to develop diagnostic criteria and to update classification criteria for the primary systemic vasculitides. By 2015 we aim to include data from over 2000 vasculitis patients and 1500 comparators.

For the development of the new Giant Cell Arteritis (GCA) classification criteria a combination of panel review and data-driven methods will be tested, comparing cases which have a submitted diagnosis of GCA with other forms of vasculitis.

C. Ponte, R. Luqmani FRI0464 Ann Rheum Dis 2014;73(Suppl2) EULAR Paris 2014
DEVELOPMENT OF THE CLASSIFICATION CRITERIA FOR GIANT CELL ARTERITIS IN THE DIAGNOSTIC AND CLASSIFICATION CRITERIA FOR VASCULITIS STUDY: A PILOT STUDY USING A PANEL REVIEW METHODOLOGY

Objectives: To test the panel review methodology in the development of the GCA classification criteria. To measure the diagnostic agreement among the panel review, and with the submitting physician, for different groups of GCA patients and comparators.

Methods: By April 2013, 1619 patients had been recruited; 821 had complete 6 month follow-up data.
DEVELOPMENT OF THE CLASSIFICATION CRITERIA FOR GIANT CELL ARTERITIS IN THE DIAGNOSTIC AND CLASSIFICATION CRITERIA FOR VASCULITIS STUDY: A PILOT STUDY USING A PANEL REVIEW METHODOLOGY

Methods: 60 cases with a submitted diagnosis of GCA and 40 cases with other forms of vasculitis as comparators (16 Takayasu arteritis, 4 Isolated aortitis, 14 Other Large-vessel vasculitis and 6 Primary CNS angiitis) were randomly extracted and developed into clinical vignettes (CV) which were assessed for diagnoses by 5 independent vasculitis experts using an online platform

For each answer a level of certainty was provided.

*C. Ponte FRI0464 Ann Rheum Dis 2014;73(Suppl2) EULAR Paris 2014*
Results: The 100 CV (67 women, 33 men) had a mean age of 63.9±16.3 years (range 21-86). The panel review agreed with the submitted diagnosis of each vasculitis sub-type in 79% of all the cases (91% agreement for GCA, 62% for comparators) with an intraclass correlation coefficient of 0.89 (CI 0.86-0.93). The panel review classified 27% of the comparators as having GCA.
Results: Temporal artery biopsy (TAB) was performed in 54 submitted GCA cases where 38 demonstrated vasculitis.

For the biopsy positive cases the review panel agreed with the diagnosis of GCA in 98% (level of certainty: definite 93%, probable 5% and possible 3%).

In the submitted GCA cases where the TAB was non-diagnostic (16) or not performed (6) the panel review agreed with this diagnosis in 81% (level of certainty: definite 9%, probable 48%, possible 40% and unlikely 3%).
Conclusions: The panel review disagreed with the submitting physician diagnosis of GCA in 9% of the cases.

This disagreement was significantly reduced in cases with positive TAB (where the prevalence of typical GCA symptoms was higher).

This exercise explores the possibility of using TAB positive cases as gold standard to derive GCA classification criteria and highlights the challenge of defining a gold standard in cases of large vessel vasculitis without biopsy confirmation of disease.
Get enrolled in a study...

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[http://www.canvasc.ca](http://www.canvasc.ca)
Conclusion

Dr. C. Pagnoux
Thank you and see you in 2015!!!
17th ANCA Workshop - 2015

http://www.vasculitis2015.org/

19-22 April 2015

Business Design Centre Islington