EUVAS update
June 5th 2012

Marinka Twilt

Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology

Submitted by Jennette et al

Reported for EUVAS meeting by N. Rasmussen



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
  - Takayasu Arteritis (TAK)
  - Giant Cell Arteritis (GCA)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
  - Polyarteritis Nodosa (PAN)
  - Kawasaki Disease (KD)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
  - AAV
    - Microscopic Polyangiitis (MPA)
    - Granulomatosis with Polyangiitis (GPA)
    - Eosinophilic Granulomatosis with Polyangiitis (EGPA)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
  - Immune complex SVV
    - Anti-GBM disease
    - Cryoglobulinemic Vasculitis
    - IgA Vasculitis (HSP)
    - Hypocomplementemic Urticarial Vasculitis
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
  - Behçet Disease (BD)
  - Cogan's Syndrome
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
  - Cutaneous Leukocytoclastic Angiitis
  - Cutaneous Arteritis
  - Primary Angiitis of the CNS (PACNS)
  - Isolated Aortitis
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
  - Lupus vasculitis
  - Rheumatoid vasculitis
  - Sarcoid vasculitis
- Vasculitis with Probable Etiology



Chapel Hill 2012 Classification

- Large Vessel Vasculitis (LVV)
- Medium Vessel Vasculitis (MVV)
- Small Vessel Vasculitis (SVV)
- Variable Vessel Vasculitis (VVV)
- Single Organ Vasculitis (SOV)
- Vasculitis Associated with Systemic Disease
- Vasculitis with Probable Etiology
  - HCV-associated cryoglobulinemic vasculitis
  - Drug-associated immune complex vasculitis
  - Drug-associated ANCA-associated Vasculitis
  - Cancer associated vasculitis



DCVAS

Diagnostic and classification criteria in Vasculitis

- prospective study to design and validate classification and diagnostic criteria in vasculitis (total sites 108!)
- still recruiting. N=1096, aiming for 4000
- data: clinical features, serology, pathology, radiology, baseline data + 6 months f-up
- Online database www.dcvas.org
- DCVAS is partner in CIHR pediatric vasculitis grant

R. Luqmani



5-year follow-up study

- 535 pts from first 4 RCTs
  - 281 MPA, 254 GPA
- 87% filled in questionnaire

Kerstin Westman



Vascular function in AAV (study1)

Single centre study vascular effects

Rituximab

- Patients: 15 AAV (rituximab), 15 AAV (CYC), 30 healthy controls (matched)
- Primary outcome: aortic pulse wave velocity
- Secondary outcomes: FMD, lipids

Alina Casian



Vascular function in AAV (study 2)

Part of Pexivas

- Immunomodulatory/ vasculoprotective effects of PLEX
- Based on removal anti-oxLDL antibodies and proinflammatory HDL, oesteopoetin, ADMA, pro-thrombotic anti-plasminogen antibodies



Renal histology

- 2 different studies
  - Anti-plasminogen antibodies at diagnosis and relation to renal histology
  - Histological determinants for long-term renal outcome



Anti-plasminogen

- anti plasminogen antibodies at diagnosis
- relation to renal biopsy
- anti-plasminogen antibodies during follow-up
- presence anti-plasminogen and renal outcome
- “new” patients (clear diagnosis according ACR criteria)
  - N=80 biopsies and sera
- “old” patients (Dx according ACR criteria not known)
  - N=70 biopsies and sera



MYCYC trial

- MMF versus CYC
- recruitment finished July 2011
- n=140 (70 MMF, 70 CYC)

- Results to be presented soon (ANCA Workshop):



PEXIVAS

Plasma exchange and glucocorticoid dosing in treatment of ANCA-associated vasculitis

- Goal inclusion 500 pt
  - 250 PLEX
    - 125 standard steroids / 125 reduced dose steroids
  - 250 no PLEX
    - 125 standard steroids /125 reduced dose steroids
- Start June 2010
- GFR < 50 ml or pulmonary hemorrhage
- 151 pt included
- 59 centers active

RITAZAREM

Superiority of fixed interval repeat rituximab against AZA for prevention relapse in AAV

- Rituximab preferred to CYC for relapses
- Relapse rate 71% in non-repeat Rituximab group (@ 24 months)
- Relapse 24% in repeat group (rituximab every 6 months)(@ 24 months)

Smith et al in press (A&R)



CORTAGE

Corticosterod-based treatment for AAV pt > 65 years of age

- FVSG study
- Reduce treatment related morbidity (death and SAE's) by 30% at 3 years (68 → 38%)
- Treatment based on Five Factor Score
  - FFS = 0 → cs alone
  - FFS > 1 → cs + iv CYC 500 mg/m²
- Experimental treatment
  - CS reduced doses
  - CYC 500 mg per pulse for all

Expected results oct 2012



MAINRITSAN

- GPA & MPA patients (FFS > 1)
- Newly diagnosed or recent relapse
- Treatment cs + CYC followed by
  - Rituximab
  - Azathioprine
- Hypothesis: absolute reduction by 25% of relapse in rituximab maintenance group
- N = 118 (last inclusion june 2010)
- Expected results oct 2012



CLEAR

C5A receptor-inhibitor on leucocytes exploratory ANCA-associated Renal vasculitis trial

- Industry trial
- CCX168 = specific human C5a-receptor antagonist
- Orally administered
- C5A = powerful neutrophil chemo-attractant and leads to pro-inflammatory cytokines
- In mice 30 mg BID → effectively blocked
- Phase I → well tolerated in healthy volunteers



CLEAR

- Phase 2
- Multinational randomized double-blind, placebo controlled phase 2 clinical trial in 39 study centers in Europe
- Primary outcome: efficacy and tolerability CCX168
- Age 18-75
- Positive ANCA/PR3/MPO
- Inclusion completed
- Step 1 of phase 2 completed (no SAE's, no rescue ivMP necessary)



BREVAS

- Belimumab in AAV
- Industry trial
- Goal n = 400
- Induction rituximab + steroids or CYC + steroids
- N = 200 belimumab + AZA
- N= 200 placebo + AZA
- Primary outcome: relapse
- Stratified by ANCA type, initial dx
- Inclusion: GPA/MPA



mepolizumab

- mepolizumab in EGPA (CSS)
- anti-Il-5 antibodies
- specific for human Il-5 (eosinophils decrease)
- 2 open label studies in EGPA
  - showed reduction steroids requirements
  - reduction exacerbations during treatment
  - well tolerated
- double blind, randomized, placebo controlled study
- treatment duration 1 year
- start 2013
- goal n = 140 (1:1 randomized)

Richard.s.philipson@gsk.com

Pediatric studies

- Brainworks and ARChiVe
- PVAS
- MYPAN



PVAS

- pediatric modification of BVAS
- 22 modified + 6 new items
- training of users
- manuscript submitted



MYPAN

- open label randomized control trial
- non-inferiority MMF to CYC for induction
- primary outcome: remission @ 6 mos
- goal n=40 (1:1 randomization)
- non-inferiority margin 15%
- bayesian approach




CANADIAN VASCULITIS NETWORK
CANVASC
2nd annual
CanVasc
meeting
Montréal, QC
November 22nd, 2012
Registration and information on
http://www.canvasc.ca



April 14 - 17 2013

16th International Vasculitis & ANCA Workshop

"Institut des Cordeliers"
Paris - France

Scientific committee :

Pr. Loïc Guillevin
(president)

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