

Kidney proteomic analysis and progression of CKD

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Conclusions of EuroKUP WG 1 - Bergamo_



Based on the WG1-2008 questionnaire responders and discussion of MC

EuroKUP consortium contains:

Laboratories with significant expertise in the proteomic analysis

Clinical research practitioners interested in various fields of kidney and urinary tract diseases

A mutual networking and collaboration - highly prioritised

Action: Allow the different members to express their interest to collaborate/or look for partners in their respective subarea of research (within the clinicians, as well as between clinicians and laboratories)

The majority of the EuroKUP partners expressed interest on:

Progression/regression of CKD

Glomerulopathy & Diabetic nephropathy

Hypertensive and ageing nephropathy

Conclusions of EuroKUP WG 1 - Bergamo_



Based on the WG1-2008 questionnaire responders and discussion of MC

Sub-classification of "renal disease":

Glomerulonephritis & Diabetic nephropathy

Tubulo-interstitial nephropathies including toxic nephropathies

Hypertensive nephrosclerosis (atherosclerotic RVD)

Polycystic kidney disease and other hereditary nephropathies

Kidney stones and metabolic kidney diseases

Kidney and urological malignancies

Actions:

Early detection of biomarkers for inflammation & fibrosis and possible retardation of progression of CKD - to be established

Centers in the net: Skopje, Sheffield, Bergamo, Athens, Gent (Vanholder), Katowice (Wiencek)

Protocol with CKD stage II pts- Prim. Glomerulonephritis

Baseline and 2 years follow up sampling

Kidney biopsy & urine (sera) sample from 24h urine

Clinical proteomics analysis of chronic kidney disease (Rationale)



CKD is becoming a global health problem

Early detection of CKD - reduce the number of patients requiring RRT

CKD diagnosed on the basis of sCr in progressed stages

CKD diagnosed by uCr at stages - sCr alone is not significantly altered

Renal biopsy - gold standard method to diagnose CKD

RB - most useful in differentiating GN (assess treatment options)

RB - no longer indicated for diagnosis of DN or NAS (esp. early CKD)

RB - no help in advanced CKD (degenerative modifications)

RB - invasive procedure - random sampling (inappropriate diagnosis)

NON-INVASIVE TOOLS

applicable to all the stages of chronic kidney disease

type of renal lesions underlying CKD

prognosis

treatment expectancies

Urinary polypeptide biomarkers for differential diagnosis and prognosis of CKD – of utmost importance

Clinical study



Objectives:

Implementing and performing the protocol in the clinical units
(approval to the ethics committee)

Providing clinical samples from around 200 patients
(urine and renal biopsy specimens collection)
(blood samples & clinical files)

Correlation of changes in tissue with primary GN with urinary
biomarkers in humans

(at which point in time of the disease development urine
biomarkers become observable and in which part of the kidney)



Clinical study

Inclusion criteria:

18-55 years of age afflicted by primary GN with established criteria for biopsy:

**(proteinuria up to 1gr/24h &/or microhematuria >10 erc)
(creatinine clearance between 60-90 ml/min - stage II)**

Exclusion criteria:

- Concomitant diabetes, hypertensive arteriopathy, multicystic disease or APKD, other systemic kidney disease
(Lupus nephritis, Wegener granulomatosis, PAN, etc.)
- obesities - BMI >30 kg/m²
- urinary tract infection or nephrolithiasis

Informed consent prior to the study recruitment !

Clinical study



Study design:

Baseline

A spot urine sample for proteomic analysis will be taken, prepared, and preserved until shipment according to previously established SOPs

24 h urine sample collection will be performed with an assessment of proteinuria, creatinine and urea

Serum samples for various biochemical parameters

Renal biopsy

At 1-year a spot and 24h urine sample as well as sera sample

Follow up after 2 years (renal biopsy, urine and sera sample)

Kidney tissue is expected in a longitudinal 2 years follow up for about 20-30 patients with primary glomerulonephritis (GN) as specific disease in each of the participating centers.

Apart from the local pathologist a centralised reading of the histology avoiding possible bias should be performed.

Clinical study



Treatment:

According to the existing guidelines for treatment of GN
specific (steroids, MMF, CyA); and/or

non-specific drugs (ACE inhibitors, ARBs, statines, RAS
blockade -Spirinolactone)

Individual CRFs:

Dose of the drugs

blood pressure

other antihypertensive treatment

Salt and protein restriction - upon the local nephrology practice
(records kept available for the study purposes)



Clinical study

Expected achievements:

Investigation of possible relationships in baseline proteomic urinary features, tissue and sera analysis and subsequent outcomes

- up & down regulations of production of various urinary biomarkers
- correlation between tissue & urinary markers
- progressors vs. non-progressors (treatment options, types, factors)

The clinical use of urinary proteins as biomarkers for:

“non-invasive prediction, diagnosis, monitoring and/or prognosis” of CKD

Defining of:

“new technologies, methodologies and approaches”

- mass screening - cheap and available methods – routine applicability