A Urinary Metabolite Constellation to Detect Acute Rejection in Kidney Allografts

1 Dept. of Nephrology, University Hospital Regensburg, Germany, 2 numares AG, Regensburg, Germany, 3 Fifth Department of Medicine, University Medical Center Mannheim, Germany, 4 Dept. of Pathology, University Hospital Erlangen, Germany

Background

Kidney transplant rejection
Routine diagnostics
- (clinical symptoms)
- GFR ↓
- urine production ↓

Confirmation by Transplant biopsy
Actual gold standard, but
- invasive
- risk of bleeding and organ damage
- maybe not representative

Requirements for an ideal biomarker
- appropriate sensitivity and specificity
- non-invasive
- quick diagnosis
- inexpensive

Safa K. et al, Curr Opin Nephrol Hypertens, 2017

Material Methods

Discovery cohort (n=1883)
- urine samples with biopsy-proven acute rejection and controls

Urine samples

NMR analysis

NMR spectra

Detected metabolite concentrations and constellations associated with rejection

Banas M et al. Metabolomics 2018

Clinical / Kidney Biomarkers and molecular changes

FG062
**Results**

**Clinical validation study:**

Urine-based metabolomic fingerprinting for assessment of the rejection risk after renal transplantation – **UMBRELLA**

- Prospective observational study
- 109 patients after kidney transplantation have been included (January 2011 - October 2013, University Hospital Regensburg)
- 1 year follow-up starting with kidney transplantation
- Study visits were identical with regular visits
- 2,479 urine samples
- 296 transplant biopsies have been performed

**renalTX-SCORE** = \(100/(1+e^{-\omega})\) with \(\omega = 0.95 \cdot C_{\text{Lactate}} + 0.25 \cdot C_{\text{Urea}} - 0.25 \cdot C_{\text{Alanine}} - 0.82 \cdot C_{\text{Citrate}} - 3.00\)

and \(C_i\) as the creatinine-normalized urine concentration of metabolite \(i\)

Banas M et al. Metabolomics 2018
Results, Discussion and Outlook

Summary

- Fast, precise and non-invasive detection of kidney transplant rejection from urine samples by NMR-Spectroscopy
- Successful prospective validation (UMBRELLA study) at the University Hospital in Regensburg
- The test showed an AUC of 0.75, which could be increased to an AUC of 0.83 by consideration of GFR
- Early detection of acute rejection 6 to 10 days before positive biopsy

Outlook

The Parasol Study

- participating centers: Regensburg, Vienna, Prague, Grenoble, Barcelona