FP7 BIOMARGIN: SMALL SETS OF URINARY CELL mRNAs LEADING TO A PARTITION TREE ON KIDNEY ALLOGRAFT LESIONS.

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Background: FP7 Biomargin aimed at detecting and validating non-invasive biomarkers of kidney graft lesions. In this study, we investigated the diagnostic potential of messenger RNAs (mRNAs) in urine samples. After screening of candidate biomarkers in a case-control study, their diagnostic performance was evaluated in a larger trans-sectional study.

Methods/Materials: Urine samples were collected at the time of protocol or for-cause biopsies in 4 European clinical centers. Patients were retrospectively selected after centralized histological reading of their biopsy by expert pathologists, and classified into 4 groups (normal, ABMR, TCMR or IF/TA). Absolute quantification of mRNAs was performed on urine cell pellets by qPCR. A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify which biomarker candidates were associated with one of the 4 groups. Multivariate models were built to define parsimonious subsets of mRNAs that collectively were highly associated with graft lesions.

Results: A total of 24 mRNAs was quantified on 238 urine cell pellets from the case-control study, which included 73 Normal, 34 TCMR, 71 IF/TA and 60 ABMR samples. A set of 4 mRNAs differentiates patients with a biopsy showing acute rejection (AMBR or TCMR) from a normal biopsy (mean AUC= 0.73). Another set of 3 mRNAs discriminates the patients with a biopsy showing acute rejection from IFTA (mean AUC=0.72). Finally, among the rejection group, a 4 gene signature enables to distinguish ABMR from TCMR (mean AUC=0.77).

Conclusion: We identified small subsets of urine mRNAs, which enable a multistep approach to discriminate patients into 4 clinically relevant situations. These non-invasive molecular signatures could advise clinicians on the indication of performing a biopsy. The diagnostic performance of our mRNA signatures is currently been investigated in a trans-sectional set of urine samples, obtained at the time of 458 consecutive biopsies. Their predictive performance will then be assessed in a prospective Cohort Study.