Results: RBT-1 was well tolerated in both healthy volunteers and subjects with CKD. The most common treatment-emergent adverse event was photosensitivity reaction (a known reaction to SnPP), which occurred in 15 subjects (27.8%) and was more commonly observed in the higher dose groups (63 and 90 mg SnPP/240 mg FeS). Photosensitivity was transient and generally mild in intensity. No serious adverse events were reported. RBT-1 related dose-dependent, statistically significant increases in cytotoxic response biomarkers in both healthy volunteers and subjects with CKD. Peak increases from baseline in healthy volunteers and subjects with CKD were: 386% and 402% for HO-1, respectively; 99% and 332% for IL-10, respectively; and 1552% and 469% for ferritin, respectively.

Conclusions: RBT-1 is well tolerated with a similar safety profile in healthy volunteers and subjects with CKD Stage 3 or 4 and elicits a biomarker response in humans that is associated with RBT-1-mediated organ protection in animal models of AKI. The positive safety and biomarker efficacy data provide a strong scientific basis to study RBT-1 as an AKI prevention strategy in patients undergoing elective cardiac surgery.

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**PO0244**

**Urinary Epidermal Growth Factor and CKD Progression: The ASSESS-AKI Study**

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**Background:** Acute kidney injury (AKI) and chronic kidney disease (CKD) are interconnected syndromes with AKI recognized as a risk factor for CKD incidence or progression. However, biomarkers of repair or resilience, such as epidermal growth factor (EGF), may help better inform this risk, given the limitations of serum creatinine (SCr) in the setting of AKI.

**Methods:** We enrolled 1,538 hospitalized patients prospectively in the multicenter Assessment, Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury (ASSESS-AKI) Study. We measured urinary epidermal growth factor (uEGF) from samples at 3 months post-discharge. The primary outcome was a composite of CKD incidence, progression, or development of end-stage kidney disease (ESKD). We also evaluated change in estimated glomerular filtration rate (eGFR) over time by EGF quartile.

**Results:** 299 (20%) patients developed the primary outcome at a median of 4.3 years follow-up. Patients in the fourth quartile of uEGF had higher eGFR at baseline and at 3-month follow-up compared to those in quartiles 1-3, as well as significantly lower albuminuria. Each 2-fold higher uEGF level was significantly associated with decreased risk of the composite outcome (HR 0.65; 95% CI: 0.59-0.71). This association remained robust after adjustment for demographic factors, baseline kidney function, urinary albumin, and other urinary biomarkers of injury and inflammation (HR 0.65, 95% CI: 0.54-0.79). Patients in uEGF quartile 1 had the fastest decline in eGFR (-5.6% per year, compared to patients in uEGF quartiles 2-4 (-3.2,-2.8,-2.3% per year, respectively).

**Conclusions:** Urinary EGF is a marker of repair after kidney injury, and higher levels of urinary discharge are associated with reduced risk of CKD and progression to ESKD in hospitalized patients with and without AKI.

**Funding:** NIDDK Support

**PO0245**

**Serum Renin and Major Adverse Kidney Events in Critically Ill Patients:**

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**Background:** Inflammatory markers of AKI have garnered attention for having potential to be sensitive biomarkers for AKI prognosis. We demonstrated that TH17 cell numbers increased in ICU patients diagnosed with AKI vs. those without AKI. The primary objective of this study was to examine the association of serum IL-17 with mortality and major adverse kidney events (MAKE) in critically ill patients with and without AKI.

**Methods:** Multicenter prospective study of 289 critically ill patients with AKI stage 2 or above, and matched ICU patients without AKI. Blood samples were collected within 48 hours after AKI diagnosis (n=153) or within 48 hours of ICU admission in those without AKI (n=146). Serum IL-17a was measured using extremely sensitive ELISA (S-Plex technology, Meso Scale Discovery). Logistic regression was used to examine the association of IL-17 levels with hospital mortality and MAKE at 90 days post-discharge (composite of death, need of renal replacement therapy or inability to recover at least 70% of baseline eGFR).

**Results:** Patients in the highest tertile of IL-17 were more severely ill than those in lower tertiles OR 2.33 (95% CI 1.73% vs. 47% vs. 33.3%, p < 0.001), more frequent mechanical ventilation (63% vs. 48% vs. 44%, p=0.021), and higher APACHE-II scores (19% vs. 15.5 vs. 14, p=0.001). Moreover, patients in the highest tertile of IL-17 had higher rates of inpatient mortality (26% vs. 8% vs. 9.1%, p=0.001) and MAKE-90. In multivariable models, patients in the highest tertile (vs. lowest tertile) had increased risk of hospital mortality (aOR 2.80, 95%CI 1.09-7.20) and MAKE-90 (aOR 3.51, 95%CI 1.72-7.14). Concordant results were obtained when IL-17 was analyzed as a continuous variable.

**Conclusions:** Higher levels of IL-17 during acute illness were independently associated with hospital mortality and MAKE-90 in critically ill patients with and without AKI. Further studies are needed to validate the use of IL-17 as a surrogate pathobiologic and prognostic marker in this susceptible population.

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