The LAPIS Trial: A Biomarker-guided Implementation of Kidney-Sparing Care Measures to Prevent Acute Kidney Injury in Sepsis Patients

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INTRODUCTION

- Acute Kidney Injury (AKI) occurs in more than half of patients in the intensive care unit (ICU), increasing morbidity and hospital costs.[1]
- Current guidelines recommend that patients be assessed for risk of AKI in order to take preventive measures.[2]
- Sepsis is the most common cause of AKI in critically ill patients and impacts 40–50% of cases.[3]
- Two urinary markers of cell-cycle arrest, tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor-binding protein-7 (IGFBP-7), have been identified as early indicators of AKI.[4,5]
- The NephroCheck® Test is a commercially available test that determines (TIMP-2)*(IGFBP7).
- The LAPIS (Limiting AKI Progression In Sepsis) trial is the first interventional, multicenter, randomized, controlled trial of sepsis subjects at risk of developing AKI.

OBJECTIVES

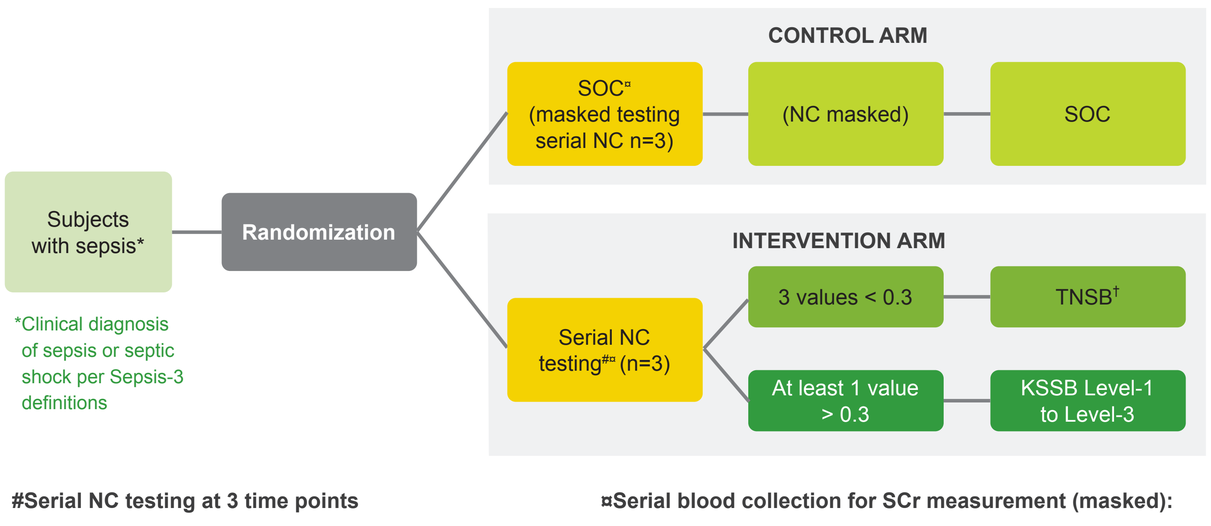
To evaluate the impact of NephroCheck-guided implementation of kidney-sparing care measures in comparison with standard of care (SOC) assessment and treatment on clinical and economic outcomes in subjects with a diagnosis of sepsis.

STUDY DESIGN

- 540 adult subjects being treated for sepsis to be enrolled
- 16 sites in the US and Europe
- Subjects will be randomized 1:1 to 1 of 2 arms:

  (1) an intervention arm utilizing serial NephroCheck testing and the implementation of NephroCheck-guided kidney sparing interventions

  (2) a control arm which will utilize standard of care assessment and treatment



*Clinical diagnosis of sepsis or septic shock per Sepsis-3 definitions

#Serial NC testing at 3 time points

T0: between 6 and 9 hours after sepsis clinical diagnosis

T1: 6-9 hrs after the first NC test

T2: 12-18 hrs after the second NC test

¤Serial blood collection for SCr measurement (masked):

3 time points T0, T1, T2 + every 12 hrs until 72 hrs

NC: NephroCheck® ; **SOC:** Standard Of Care ; **TNSB:** Test Negative Sepsis Bundle ; **KSSB:** Kidney Sparing Sepsis Bundle

†TNSB will only be followed for subjects with no evidence of AKI by creatinine and UO (Urine Output).

LAPIS INTERVENTIONS

3 values < 0.3 + no evidence of AKI

TNSB

- Removal of the Foley catheter
- Spacing SCr to daily
- No/removal of hemodynamic monitoring
- Permissive use of NSAIDs/ACE inhibitors/ diuretics
- Transfer out of the ICU (e.g. to floor or step-down unit)

At least 1 value > 0.3

KSSB Level-1

- Discontinue all nonessential nephrotoxic agents
- For vancomycin or aminoglycosides, dosing should be based upon therapeutic drug level monitoring
- Review all medications with a clinical pharmacist
- Strict measurement of fluids in/out
- Consider alternatives to radiocontrast procedures

KSSB Level-2

- Institute functional hemodynamic monitoring to optimize the volume status and hemodynamic parameters

KSSB Level-3

- Consult Nephrology and Infectious Disease
- Seek other source of infection

3 levels of care following a specific algorithm

LAPIS OUTCOMES

- **Primary endpoint:**
  - Composite endpoint of death, dialysis or progression of 2 or more stages of AKI (stage 0 to 2/3 or stage 1 to 3) within 72 hours after enrollment in the intervention arm compared with the control arm
- Additional endpoints will include hospital and ICU length of stay, 30-day readmission rates and other health-economic endpoints

CONCLUSION

- LAPIS is a novel biomarker-guided interventional trial in sepsis patients at risk of AKI
- Enrollment is planned to start in March 2020 with 18 month enrollment period
- The site selection process is ongoing

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LAPIS
Limiting AKI Progression In Sepsis

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