Selected Definitions

Duration of Adequate Treatment

The duration of adequate treatment will be defined as the number of cumulative days during which the patient receives an antibiotic to which the index blood culture isolate(s) is/are all susceptible. The total duration may include multiple adjacent (or overlapping) courses of different antimicrobials. A day of adequate treatment will be a day on which the patient receives at least one effective agent (including dosing intervals greater than 24 hours when antibiotic clearance is impaired due to renal or hepatic dysfunction). In the primary analysis, the total duration can extend back only as far as the date of the blood culture collection.

Definitions for Secondary Outcomes

- **Hospital all cause *mortality***: recorded as alive or dead at hospital discharge following index positive blood culture.
- **ICU all cause *mortality***: recorded as alive or dead at ICU discharge following index positive blood culture.
- **Relapse Rate of bacteremia:** defined as the recurrence of bacteremia due to original infecting organism (same Genus and species) after documentation of negative blood cultures or clinical improvement and within 30 days after completing course of adequate antimicrobial therapy.
- **Intensive care unit length of stay** - defined as the duration between index blood culture and discharge from the ICU for a consecutive 48-hour period. Durations will be calculated for all patients then separately for patients who died within hospital and those who did not die.
- **Hospital length of stay** – defined as the duration between index blood culture and discharge date from hospital. Durations will be calculated for all patients then separately for patients who died within hospital and those who did not die.
- **Duration of mechanical ventilation** – defined as the number of consecutive days receiving invasive (via an endotracheal tube or tracheostomy), or non-invasive (via a facemask, nasal mask, or helmet) ventilation. Durations will be calculated for all patients then separately for patients who died within hospital and those who did not die.
- **Duration of vasopressor use** - defined as the number of consecutive days receiving intravenous vasoactive medications (e.g. epinephrine, norepinephrine, vasopressin, dopamine, phenylephrine, dobutamine, milrinone). Durations will be calculated for all patients then separately for patients who died within hospital and those who did not die.
- **Antibiotic-free days** - defined as the number of days during the 28 days after the start of adequate antibiotics in which patients did not receive any antibiotics. This definition will include all antibiotics, irrespective of their activity against the pathogen(s) in the initial blood culture.
- **Antibiotic allergy and adverse events**

- **Anaphylaxis**: To be considered anaphylaxis, the patient must have had ≥1 of the following 3 criteria that a medical team member attributed to an Antimicrobial
    - Acute onset of skin or mucosal tissue changes (hives, itching/flush, lip/tongue/uvula swelling) over minutes/hours, accompanied by
        - respiratory compromise (dyspnea, wheeze, stridor, hypoxemia), AND/OR
        - reduced blood pressure or symptoms/signs of end organ dysfunction from shock
    - Rapid onset of two or more of the following
        - involvement of the skin-mucosa (hives, itch//flush, swollen lips/tongue/uvula)
        - respiratory compromise
        - reduced blood pressure or associated symptoms/signs
        - persistent gastrointestinal symptoms/signs (crampy abdominal pain, vomiting)
    - Reduced blood pressure after exposure to a known allergen for that patient

- **Antimicrobial-associated renal injury**: To be considered Antimicrobial-associated renal injury, a medical team member must have attributed the renal injury to the Antimicrobial, and the severity of the renal injury must meet one of these (RIFLE criteria):
    - Risk: GFR decrease >25%, serum creatinine increased 1.5 times or urine production of <0.5 ml/kg/hr for 6 hours
    - Injury: GFR decrease >50%, doubling of creatinine or urine production <0.5 ml/kg/hr for 12 hours
    - Failure: GFR decrease >75%, tripling of creatinine or creatinine >355 µmol/l (with a rise of >44) (>4 mg/dl) OR urine output below 0.3 ml/kg/hr for 24 hours
    - Loss: persistent AKI or complete loss of kidney function for more than 4 weeks
    - End-stage renal disease: need for renal replacement therapy (RRT) for more than 3 months
- **Antimicrobial-associated hepatitis**: To be considered Antimicrobial-associated hepatitis, a medical team member must have attributed the hepatitis to the Antimicrobial, and the severity of the hepatitis must meet this FDA criteria for hepatic adverse events:
    - ALT> 3x the upper limit of normal

- ***Risk of Clostridium difficile***– defined as a positive PCR or ELISA test for *Clostridium difficile* toxin in the context of diarrhea within hospital (or 90 days, whichever arrives first) of bacteremia diagnosis.
- **Risk of colonization/infection with antimicrobial resistant organisms in hospital**– defined as a positive culture yielding a highly resistant microbial organism (HRMO) as

defined by the Dutch nosocomial infection surveillance guidelines [*de Smet, Lancet ID, 2011: 11: 372-80*]. This broad definition includes methicillin-susceptible Staphylococcus aureus, vancomycin-resistant Enterococci, extended spectrum beta-lactamase producing Enterobacteriaceae, carbapenem-resistant Gram negative bacilli, and multi-drug resistant Gram negative bacilli (with definition of multi-drug resistance differing according to Enterobacteriaceae and non-Enterobacteriaceae species). We will also conduct a sensitivity analysis limited to isolation of these organism(s) only from sterile site specimens (such as blood, cerebrospinal fluid, peritoneal fluid, synovial fluid, pleural fluid, and tissue biopsies).

- **Antibiotic resistant organism-** defined as highly resistant microorganisms that include: methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococci spp, extended spectrum beta-lactamase producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, carbapenem-resistant Acinetobacter spp; or Enterobacteriaceae resistant to at least two of fluoroquinolones, aminoglycosides or trimethoprim-sulfamethoxazole, Acinetobacter spp resistant to at least two of fluoroquinolones, aminoglycosides or ceftazidime; or non-Enterobacteriaceae resistant to at least three of fluoroquinolones, aminoglycosides, carbapenems, ceftazidime or piperacillin.