# Supplemental file 2 - Schedule of Activities

The schedule of activities (SoA), as outlined in Table 3, consists of a Pre-treatment Period, a Treatment Period and a Follow-up Period.

| | Pre-treatment Period | | Treatment period | | | Follow-up period*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Assessments** | **Screening** | **Baseline*** | **Day 1**** | **Day 2** | **Day 3** | **Day 4** | **Day 5** | **Day 6** | **Day 7** | **Day 28 (+4 days)** | **Day 90 (+10 days)** | **Day 180 (+10 days)** | **EOT (in case of withdrawal)** |
| **Eligibility check (inclusion/exclusion criteria)** | X | | | | | | | | | | | | |
| **Informed consent** | X | | | | | | | | | | | | |
| **Pregnancy test (urine or blood), WOCBP only[6]** | X | | | | | | | | | | | | |
| **Serum/plasma CR[1]** | | X | Daily until ICU or intermediate care unit discharge (max to Day 7) | | | | | | | X | X | | |
| **KDIGO AKI Stage** | | X | Daily until ICU or intermediate care unit discharge (max to Day 7) | | | | | | | X | X | | |
| **Medical history[2]** | | X | | | | | | | | | | | |
| **Demographics** | | X | | | | | | | | | | | |
| **Weight, height[3]** | | X | | | | | | | | | | | |
| **12-lead ECG** | | X | | | | | | | | | | | |
| **mSOFA score[4]** | | X | Daily until ICU or intermediate care unit discharge (max to Day 7) | | | | | | | | | | |
| **APACHE II (incl. GCS)** | | X | | | | | | | | | | | |
| **Main cause of sepsis[5]** | | X | | | | | | | | | | | |
| **Hematology[7]** | | X | | | X | | | | | X (or at hospital discharge if before Day 28) | | | X[8] |
| **Clinical chemistry[7]** | | X | | | X | | | | | X (or at hospital discharge if before Day 28) | | | X[8] |
| **Blood sampling Biomarkers[9]** | | X | X | X | X | X | X | | | X | | | |
| **Blood sample for ADA[9,10]** | | X | | | | | | | | X | X | | X |
| **Randomization[11]** | | X | | | | | | | | | | | |
| **Trial drug administration[12]** | | | X | X | X | | | | | | | | |
| **PK samples[13,9]** | | | | | X | X | X | | X | | | | |

| | Pre-treatment Period | | Treatment period | | | Follow-up period*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Assessments** | **Screening** | **Baseline*** | **Day 1**** | **Day 2** | **Day 3** | **Day 4** | **Day 5** | **Day 6** | **Day 7** | **Day 28 (+4 days)** | **Day 90 (+10 days)** | **Day 180 (+10 days)** | **EOT (in case of withdrawal)** |
| **Urine samples for purine determination[14]** | | X | X | X | X | X | | | | | | | |
| **Functional Status and Residency[15]** | | X | | | | | | | | X | X | X | |
| **QoL EQ-5D-5L[16]** | | X | | | | | | | | X | X | X | |
| **Mechanical ventilation [17]** | | X | | | | | | | | | | | |
| **Vasopressor/ Inotropic use[18]** | | X | | | | | | | | | | | |
| **Renal replacement therapy[19]** | | X | | | | | | | | | X | | |
| **Prior and concomitant medication[20]** | | X (until hospital discharge) | | | | | | | | | | | |
| **AE[21]** | | X | | | | | | | | | | | |
| **ICU/hospital admission /discharge[22]** | | X | | | | | | | | | | | |
| **Rehospitalization[23]** | | X | | | | | | | | | | | |
| **Mortality[24]** | | X | | | | | | | | | | | |

Abbreviations: ADA = anti-drug antibodies; AE = adverse events; AP = alkaline phosphatase; APACHE II = Acute Physiology and Chronic Health Evaluation II; CR = creatinine; ECG = electrocardiogram; eCRF = electronic case report forms; EOT = end of trial; GCS: Glasgow Coma Scale; ICU = intensive care unit; KDIGO AKI = Kidney Disease Improving Global Outcomes acute kidney injury; mSOFA = modified Sequential Organ Failure Assessment; MV = mechanical ventilation; PK = pharmacokinetic; QoL EQ-5D-5L = Quality of Life EuroQoL-5-Dimensions-5 Levels; SA-AKI = sepsis-associated acute kidney injury; RRT = renal replacement therapy; SAE = serious adverse event; SOFA = Sequential Organ Failure Assessment; WOCBP = women of child bearing potential.

* Assessments performed for clinical purposes before start of infusion of trial drug may be used as Baseline if deemed appropriate.

** If Day 1 and Baseline occur on the same calendar day, there is no requirement to do trial specific assessments on Day 1 after trial drug administration. Results of assessments done for clinical purposes on Day 1 after trial drug administration should be entered in the eCRF.

*** The follow-up assessments may be performed in the hospital for patients still in the hospital or able to come to the hospital after discharge or at home if the patient is not able to attend after discharge. Home visits can be performed by trial personnel, if allowed by local regulations, or by a third-party vendor.

1 Performed by local laboratory. If multiple CR values are available on the day of Baseline, the value closest to the time of randomization should be recorded. If Day 1 and Baseline is on the same calendar day, there is no requirement to repeat measurements on Day 1 after trial drug administration. From Day 2 onwards, if more than one CR value is available on a single day, the worst daily value should be recorded.

2 Medical history will be collected by using the Charlson co-morbidity index supplemented with recent medical history of relevance to this episode of SA-AKI including whether the reason for ICU admission is medical, surgical or trauma.

3 Known hospital admission weight or estimated weight and height can be used. Weight in kg will be used for trial drug reconstitution.

4 mSOFA (i.e., excluding the Glasgow Coma Score) is to be obtained daily from Baseline to Day 7. On days where hematology and clinical chemistry measurements are required as part of safety measurements, these results can be used for the mSOFA score. On days where hematology and clinical chemistry measurements are not required, the platelets, bilirubin, and CR must be measured by the local laboratory to calculate a mSOFA score. If the patient is discharged from the ICU or intermediate care unit before

Day 7, mSOFA need not be collected. At Baseline, mSOFA must be available before randomization for stratification. If Day 1 and Baseline is on the same calendar day, mSOFA does not need to be obtained again on Day 1 after trial drug administration.
5 Record, when available. See Section 8.3.2.8 for specific information to be recorded.
6 Performed by local laboratory. Both urine and blood pregnancy tests are allowed. Only to be performed for WOCBP.
7 Performed by local laboratory, see Section 8.3.4.2. AP activity should not be measured during the first 14 days after the first trial drug administration or results from blood samples taken during the first 14 days of the trial are not to be reported to trial team members or to any other blinded personnel involved in patient care and/or data collection as it could lead to unblinding and to erroneous interpretation of liver function, as the recAP administered will increase the AP activity. Blinding plans will be made and approved for each site before the start of the trial and must be followed.
8 Only to be performed if patient withdraws before Day 28 (inclusive).
9 Handling, storing and shipment of the samples is described in the Laboratory Manual.
10 ADA Samples taken on Day 90 will only be analyzed in case of a positive result on Day 28. At Day 180 and Day 360, a blood sample for ADA will only be taken in patients with a positive ADA response on Day 90 and Day 180, respectively. Collection of ADA sample for patients withdrawn are only required if EOT visit takes place after Day 28 and before Day 90. Handling, storing and shipment of the samples is described in the Laboratory Manual.
11 mSOFA score must be available for the stratification at randomization.
12 On Day 2 and Day 3, trial drug administration should start 24 +/- 2 hours after the previous trial drug administration.
13 On Day 3, a PK sample must be collected before trial drug administration and another sample 2.5 - 3.5 hours after the start of the infusion. On Day 4, Day 5, and Day 7, PK samples can be taken at any time. The exact date and time of blood draw must be recorded in the eCRF.
14 In patients at selected sites, a daily urine sample will be collected at Baseline up to Day 4. At the dosing days (Day 1, Day 2 and Day 3), the urine sample must be taken within one hour after the end of trial drug administration. On Day 4, urine collection can be performed at any time. Handling, storing and shipment of the samples is described in the Laboratory Manual.
15 Functional status and residence at Baseline will be a recall of the patient's situation prior to hospitalization for SA-AKI.
16 Baseline refers to a recall of the patient's quality of life before the current SA-AKI episode. If a patient is not able to perform the QoL at Baseline (e.g., due to sedation), the patient should complete the baseline QoL when his/her medical condition allows it. If a patient is unable to complete the EQ-5D-5L questionnaires themselves, the questionnaire can be completed by an interview by reading the questions and answers objectively. If the patient is discharged from hospital, the questionnaire may be completed by a phone interview.
17 Mechanical ventilation (MV) is defined as any positive pressure ventilation via endotracheal or tracheostomy tube or any non-invasive ventilation with >5 cm H2O pressure. Record MV start and stop dates together with information on the modality/modalities.
18 Record the start and stop time and date for each inotropic and vasopressor drug.
19 All renal replacement therapy (RRT) modalities (continuous, intermittent and non-continuous) are allowed in the trial. Up to Day 28, record the main reason to start RRT, the modality, and start and stop date in the eCRF. At Day 90, record the RRT status.
20 Relevant prior and concomitant medication should be collected up to and including Day 28 or until hospital discharge if before Day 28. Concomitant medications/procedures that are likely to influence the outcome of the SA-AKI and nephrotoxic drug have to be detailed. See Section 6.5 for more details.
21 Safety is followed up until Day 28 (inclusive). However, ongoing SAE's on Day 28 will be followed until resolution or until they have reached a stable medical condition.
22 ICU or intermediate care unit and hospital admission and discharge dates as well as reason for admissions must be recorded.
23 Rehospitalization is defined as an overnight stay in any hospital.
24 Record date and cause of death on a separate eCRF page. Cause of any death occurring up to and including Day 28 will additionally be recorded as an SAE.