

Appendix

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

Proposed presentation of data for the STARRT-AKI Trial

Posted online on XX 201X (prior to completion of enrolment)

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SUPPLEMENTAL TABLES

Table S1: Characteristics at enrollment.

Table S2: Characteristics of RRT prescription.

Table S3: Characteristics at RRT initiation.

Table S4: Subgroup analyses.

Table S5: Cause of death.

Table S6: Subgroup analysis on the primary outcome by country.

Table S1: Characteristics at enrollment

Characteristics	Accelerated strategy (N=xxxx)	Standard strategy (N=xxxx)
Clinical parameters		
Clinical Frailty Scale score	xx (xx-xx)	xx (xx-xx)
EQ-VAS	xx (xx-xx)	xx (xx-xx)
Physiological parameters		
Heart rate – beats/min	xxx (xx.x)	xxx (xx.x)
Systolic blood pressure – mmHg	xxx (xx.x)	xxx (xx.x)
Temperature – degrees Celsius	xxx (xx.x)	xxx (xx.x)
Glasgow coma scale	xx (xx)	xx (xx)
Oliguria or anuria – no. (%)	xxx (xx.x)	xxx (xx.x)
Urine output – mL/24 hour	xxx (xx.x)	xxx (xx.x)
Fluid balance – mL/24 hour	xxx (xx.x)	xxx (xx.x)
Laboratory parameters		
Serum creatinine (baseline) – mg/dl	xxx (xx.x)	xxx (xx.x)
Estimated GFR – mL/min/1.73m ²	xxx (xx.x)	xxx (xx.x)
Serum creatinine (enrolment) – md/dl	xxx (xx.x)	xxx (xx.x)
Blood urea nitrogen – mg/dl	xxx (xx.x)	xxx (xx.x)
Serum sodium – mmol/litre	xxx (xx.x)	xxx (xx.x)
Serum potassium – mmol/litre		
Serum bicarbonate – mmol/litre	xxx (xx.x)	xxx (xx.x)
Arterial pH	x.x (x.x)	x.x (x.x)
Serum bilirubin – mg/dl	xxx (xx.x)	xxx (xx.x)
Serum hemoglobin – g/dl	xxx (xx.x)	xxx (xx.x)
White blood cell count – cells x 10 ⁹ /l	xxx (xx.x)	xxx (xx.x)
Serum platelets – cells x 10 ⁹ /l	xxx (xx.x)	xxx (xx.x)
Support and interventions – no. (%)		
Mechanical ventilation	xxxx (xx.x)	xxxx (xx.x)
Vasoactive support	xxxx (xx.x)	xxxx (xx.x)
Diuretic therapy	xxxx (xx.x)	xxxx (xx.x)
Enteral nutrition	xxxx (xx.x)	xxxx (xx.x)
TPN	xxxx (xx.x)	xxxx (xx.x)

Abbreviations: EQ-VAS = EuroQol visual analogue scale; TPN = total parenteral nutrition.

Table S2: Characteristics of RRT prescription

Characteristic	Accelerated strategy (N=xxxx)	Standard strategy (N=xxxx)	P value
RRT initiated – no. (%)	xxxx (xx.x)	xxxx (xx.x)	x.xxx
Time from eligibility to RRT initiation – hours	xx (xx–xx)	xx (xx–xx)	x.xxx
Time from randomization to RRT initiation – hours	xx (xx–xx)	xx (xx–xx)	x.xxx
Dialysis catheter insertion site – no. (%)			
Jugular	xxxx (xx.x)	xxxx (xx.x)	x.xxx
Femoral	xxxx (xx.x)	xxxx (xx.x)	x.xxx
Subclavian	xxxx (xx.x)	xxxx (xx.x)	x.xxx
Initial RRT modality – no. (%)			
IHD	xxxx (xx.x)	xxxx (xx.x)	x.xxx
SLED	xxxx (xx.x)	xxxx (xx.x)	x.xxx
CRRT	xxxx (xx.x)	xxxx (xx.x)	x.xxx
RRT dose-intensity prescribed			
IHD – hours	xx (x.x)	xx (x.x)	x.xxx
SLED – hours	xx (x.x)	xx (x.x)	x.xxx
CRRT – mL/kg/hr	xx (x.x)	xx (x.x)	x.xxx
Anticoagulation – no. (%)			
Heparin	xx (x.x)	xx (x.x)	x.xxx
Citrate	xx (x.x)	xx (x.x)	x.xxx
None	xx (x.x)	xx (x.x)	x.xxx
Ultrafiltration - mL	xx (x.x)	xx (x.x)	x.xxx

Abbreviations: RRT = renal replacement therapy; IHD = intermittent hemodialysis; SLED = slow low efficiency dialysis; CRRT = continuous renal replacement therapy

Table S3: Characteristics at RRT initiation.		
Criteria – no. (%)	Accelerated strategy (N=xxxx)	Standard strategy (N=xxxx)
RRT initiated – no. (%)	xxxx (xx.x)	xxxx (xx.x)
Time from eligibility to RRT initiation – hours	xx (xx–xx)	xx (xx–xx)
Time from randomization to RRT initiation – hours	xx (xx–xx)	xx (xx–xx)
SOFA score	xx (x.x)	xx (x.x)
Physiological parameters		
Heart rate – beats/min	xxx (x.x)	xxx (x.x)
Systolic blood pressure – mmHg	xxx (x.x)	xxx (x.x)
Respiratory rate – breaths/minute	xx (x.x)	xx (x.x)
PaO ₂ /FiO ₂ ratio	xx (xx)	xx (xx)
Urine output in the preceding 24 hours – mL	xxx (xx.x)	xxx (xx.x)
Fluid balance – mL	xxx (xx.x)	xxx (xx.x)
Laboratory parameters		
Serum creatinine (baseline) – mg/dl	xxx (xx.x)	xxx (xx.x)
Serum creatinine (enrolment) – md/dl	xxx (xx.x)	xxx (xx.x)
Serum creatinine (RRT initiation) – md/dl	xxx (xx.x)	xxx (xx.x)
Blood urea nitrogen – mg/dl	xxx (xx.x)	xxx (xx.x)
Serum potassium – mmol/litre	xxx (xx.x)	xxx (xx.x)
Serum bicarbonate – mmol/litre	xxx (xx.x)	xxx (xx.x)
Arterial pH	x.x (x.x)	x.x (x.x)
Serum hemoglobin – g/dl	xxx (xx.x)	xxx (xx.x)
Criteria for RRT initiation met – no. (%)		
Yes	-	xxxx (xx.x)
No	-	xxxx (xx.x)
Clinician-reported Reason for RRT initiation if criteria not met – no. (%)		
Volume overload	-	xxxx (xx.x)
Oliguria/anuria	-	xxxx (xx.x)
Creatinine increasing/AKI worsening	-	xxxx (xx.x)
Other	-	xxxx (xx.x)

Abbreviations: RRT = renal replacement therapy; AKI = acute kidney injury; SOFA = sequential organ failure assessment.

Table S4. Subgroup analyses

	Accelerated strategy (N=xxxx)	Standard strategy (N=xxxx)	Odds Ratio (95% CI)	Interaction P value
Mortality at 90-days – no. (%)				
Patient sex				x.xx
Female	xx (xx.x)	xx (xx.x)	x (x-x)	
Male	xx (xx.x)	xx (xx.x)	x (x-x)	
Patients with eGFR < 45 ml/min/1.73m ²				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Patients with SAPS II score > xx				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Patient surgical status				x.xx
Medical	xx (xx.x)	xx (xx.x)	x (x-x)	
Surgical	xx (xx.x)	xx (xx.x)	x (x-x)	
Patients with sepsis				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Geographic region				x.xx
North America	xx (xx.x)	xx (xx.x)	x (x-x)	
Europe	xx (xx.x)	xx (xx.x)	x (x-x)	
Australia/New Zealand	xx (xx.x)	xx (xx.x)	x (x-x)	
Asia/South America	xx (xx.x)	xx (xx.x)	x (x-x)	

Table S5: Causes of death.

Cause	Accelerated strategy (N=xxxx)	Standard strategy (N=xxxx)	P value
Neurological – no. (%)			
Brain death	xx (x.x)	xx (x.x)	x.xxx
Hypoxic encephalopathy	xx (x.x)	xx (x.x)	x.xxx
Intracranial haemorrhage	xx (x.x)	xx (x.x)	x.xxx
Ischemic stroke	xx (x.x)	xx (x.x)	x.xxx
Other	xx (x.x)	xx (x.x)	x.xxx
Cardiovascular – no. (%)			
Primary arrhythmia	xx (x.x)	xx (x.x)	x.xxx
Refractory cardiogenic shock	xx (x.x)	xx (x.x)	x.xxx
Cardiac tamponade	xx (x.x)	xx (x.x)	x.xxx
Hypovolemia (bleeding)	xx (x.x)	xx (x.x)	x.xxx
Septic shock	xx (x.x)	xx (x.x)	x.xxx
Massive pulmonary embolism	xx (x.x)	xx (x.x)	x.xxx
Anaphylaxis	xx (x.x)	xx (x.x)	x.xxx
Other	xx (x.x)	xx (x.x)	x.xxx
Respiratory – no. (%)			
Refractory hypoxia due to ARDS	xx (x.x)	xx (x.x)	x.xxx
COPD	xx (x.x)	xx (x.x)	x.xxx
Asthma	xx (x.x)	xx (x.x)	x.xxx
Pulmonary haemorrhage	xx (x.x)	xx (x.x)	x.xxx
Pneumothorax	xx (x.x)	xx (x.x)	x.xxx
Other	xx (x.x)	xx (x.x)	x.xxx
Metabolic – no. (%)			
Hypoglycaemia	xx (x.x)	xx (x.x)	x.xxx
Hyperkalemia	xx (x.x)	xx (x.x)	x.xxx
Hypothermia	xx (x.x)	xx (x.x)	x.xxx
Liver failure	xx (x.x)	xx (x.x)	x.xxx
Other	xx (x.x)	xx (x.x)	x.xxx

Table S6. Subgroup analysis on the primary endpoint by country.*

Country (no. sites)	Accelerated strategy (N=xxxx)	Standard strategy (N=xxxx)	Odds Ratio (95% CI)	Interaction P value
Mortality at 90-days – no. (%)				
Australia (16)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Austria (4)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Brazil (1)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Belgium (1)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Canada (40)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
China (14)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
France (29)				x.xx
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	

Finland (3)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Germany (2)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Ireland (1)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Italy (2)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
New Zealand (9)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
Switzerland (2)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
United Kingdom (32)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
United States (6)				X.XX
Yes	xx (xx.x)	xx (xx.x)	x (x-x)	
No	xx (xx.x)	xx (xx.x)	x (x-x)	
* As of June 24, 2019				

FIGURES

Figure 2. Kaplan-Meier survival estimates of the probability of survival to Day 90

Description: Line graph with days 0 to 90 on the horizontal axis and probability of survival on the vertical axis. Patients at risk by group will be described below the graph.

Figure 3. Kaplan-Meier survival estimates of the probability of renal replacement therapy (RRT)-free to Day 90

Description: Line graph with Days 0–90 on the horizontal axis and probably of being free from RRT treatment on the vertical axis. Patients at risk by group will be described below the graph.

Figure 4. Forest plot of treatment effect stratified by treatment allocation across a priori subgroups

SUPPLEMENTAL FIGURES

Figure S1: Change in serum creatinine and blood urea nitrogen over time.

Description: Boxplot graph with days 0 to 14 on the horizontal axis and creatinine and blood urea nitrogen on the vertical axis.

Figure S2: Change in fluid balance over time.

Description: Boxplot graph with days 0 to 14 on the horizontal axis and fluid balance on the vertical axis.

Figure S3: Time from randomization to the initiation of RRT

Description: Line graph with days 0 to 90 on the horizontal axis and proportion free from RRT on the vertical axis.