Proposed presentation of data for Mega-ROX Sepsis

Version 1. 4th October 2022

Table 1: Baseline characteristics

Characteristic	Conservative oxygen therapy (n=xxxx)	Liberal oxygen therapy (n=xxxx)
Age – yr	xx.x ± xx	xx.x ± xx
Male sex – no. (%)	xxx (xx.x)	xxx (xx.x)
Body mass index	xx.x ± xx	xx.x ± xx
Clinical frailty score	xxx (xx.x)	xxx (xx.x)
Source of admission to ICU – no. (%)		
Emergency department	xxx (xx.x)	xxx (xx.x)
Hospital ward	xxx (xx.x)	xxx (xx.x)
Transfer from another ICU	xxx (xx.x)	xxx (xx.x)
Transfer from another hospital (except from another ICU)	xxx (xx.x)	xxx (xx.x)
From OT following surgery	xxx (xx.x)	xxx (xx.x)
Hours from hospital admission to randomisation	xx.x ± xx	xx.x ± xx
Hours from ICU admission to randomisation	xx.x ± xx	xx.x ± xx
APACHE-II score*	xx.x ± xx	xx.x ± xx
SAPS-III score†		
Sepsis source – no. (%)		
Respiratory	xxx (xx.x)	xxx (xx.x)
Gastrointestinal	xxx (xx.x)	xxx (xx.x)
Genitourinary	xxx (xx.x)	xxx (xx.x)
Musculoskeletal and skin	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)
COVID-19 – no. (%)	xxx (xx.x)	xxx (xx.x)
Baseline oxygen data		
FiO_2	xx.x ± xx	xx.x ± xx
PaO_2 – mmHg	xx.x ± xx	xx.x ± xx
PaO_2/FiO_2 ratio – mmHg	xx.x ± xx	xx.x ± xx

Plus-minus values will be expressed as mean ± SD (where the distribution of the data is not normal, median [IQR] will be reported instead of mean ± SD). To facilitate meaningful interpretation of categorical variables, categories with small numbers (<10) will be collapsed for analysis.

* Scores on the APACHE II range from 0 to 71, with higher scores indicating more severe disease and a higher risk of death.

† Scores on the SAPS-III range from 0 to 217, with higher scores indicating more severe disease. The SAPS-III score was collected from trial participants from Brazil.

Abbreviations: APACHE: Acute Physiology And Chronic Health Evaluation; CNS: Central Nervous System; ICU: Intensive Care Unit; OT: operating theatre; SpO_2: arterial oxygen saturation on pulse oximetry; PaO_2: arterial partial pressure of oxygen; FiO_2: fraction of inspired oxygen; $PaCO_2$: arterial partial pressure of carbon dioxide; PEEP: positive end expiratory pressure.

Table 2: Oxygen exposure by treatment group

Oxygen exposure metric – n (%)	Conservative oxygen therapy (n=xxx)	Liberal oxygen therapy (n=xxx)	Between-Group difference (95% CI)
Median [IQR] percentage of hours per patient SpO_2 ≥97%	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Median [IQR] number of hours per patient SpO_2 ≥97%	xx (xx.x)	xx (xx.x)	xx (xx to xx)
Median [IQR] percentage of hours per patient SpO_2 <88%	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Median [IQR] number of hours per patient SpO_2 <88%	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Proportion of patients with at least one PaO_2 recording <60mmHg	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Proportion of patients with at least one PaO_2 recording >100mmHg	xx (xx.x)	xx (xx.x)	xx (xx to xx)
Median [IQR] percentage of hours per patient FIO_2 0.21	xx (xx.x)	xx (xx.x)	xx (xx to xx)
Median [IQR] number of hours per patient FIO_2 0.21	xx (xx.x)	xx (xx.x)	xx (xx to xx)

Abbreviations: IQR: Interquartile range; CI: Confidence Interval

Table 3: Outcomes

	Conservative oxygen therapy (n=xxxxx)	Liberal oxygen therapy (n=xxxxx)	Estimate (95% CI)
Primary outcome*			
Died at the hospital by day 90- no. (%)	xxxx (xx.x)	xxxx (xx.x)	**Relative risk** xx (xx to xx) **Risk difference** xx (xx to xx)
Secondary outcomes			
Hours until removed alive from invasive mechanical ventilation			**Subhazard ratio of time to extubation‡**
Number of patients	xxxxx	xxxxx	
Median (IQR)†	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Days until discharged alive from ICU			**Subhazard ratio of time to ICU discharge‡**
Number of patients	xxxxx	xxxxx	
Median (IQR)†	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Days until discharged alive from hospital			**Subhazard ratio of time to Hospital discharge‡**
Number of patients	xxxxx	xxxxx	
Median (IQR)†	xx (xx-xx)	xx (xx-xx)	xx (xx to xx)
Discharged home- no. (%)	xxxxx (xx.x)	xxxxx (xx.x)	**Relative risk** xx (xx to xx) **Risk difference** xx (xx to xx)
Day-90 mortality- no. (%)	xxxx (xx.x)	xxxx (xx.x)	**Relative risk** xx (xx to xx) **Risk difference** xx (xx to xx)

Abbreviations: IQR: Interquartile range; CI: Confidence Interval

* A P-value for the primary outcome comparison will be shown in a footnote. The absolute difference in 90 day mortality and corresponding relative risk will be adjusting for site and for the presence or absence of each of the following at randomisation: suspected hypoxic ischaemic encephalopathy following resuscitation from a cardiac arrest, and acute brain pathologies other than hypoxic ischaemic encephalopathy.

† Duration of invasive mechanical ventilation and ICU and hospital length of stay will be calculated from cumulative incidence functions with mortality regarded as a competing risk.

‡ Ratios of median time to discharge (or extubation) will be estimated using censored linear regression with logarithm of time to discharge (or extubation) as the dependent variable. Adjustment will be made for the same variables as for the primary outcome.

Table S1: Causes of respiratory sepsis*		
Sepsis source	**Conservative oxygen therapy (n=xxxx)**	**Liberal oxygen therapy (n=xxxx)**
Respiratory sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Respiratory sinus infection	xxx (xx.x)	xxx (xx.x)
Tonsil or pharyngeal infection	xxx (xx.x)	xxx (xx.x)
Epiglottitis	xxx (xx.x)	xxx (xx.x)
Pertussis	xxx (xx.x)	xxx (xx.x)
Croup or laryngotracheobronchitis (non-influenza)	xxx (xx.x)	xxx (xx.x)
Acute bronchitis, non-influenza	xxx (xx.x)	xxx (xx.x)
Infective exacerbation of COPD	xxx (xx.x)	xxx (xx.x)
Bronchiectasis	xxx (xx.x)	xxx (xx.x)
Bacterial pneumonia	xxx (xx.x)	xxx (xx.x)
Viral pneumonia, non-influenza (include COVID-19)	xxx (xx.x)	xxx (xx.x)
Influenza	xxx (xx.x)	xxx (xx.x)
Fungal or yeast pneumonia	xxx (xx.x)	xxx (xx.x)
Parasitic pneumonia	xxx (xx.x)	xxx (xx.x)
Pneumonia, no organism isolated	xxx (xx.x)	xxx (xx.x)
Lung abscess	xxx (xx.x)	xxx (xx.x)
Tuberculosis	xxx (xx.x)	xxx (xx.x)
Empyema or infected effusion	xxx (xx.x)	xxx (xx.x)
Pleurisy	xxx (xx.x)	xxx (xx.x)

* Where it is logical to combine categories, those with small numbers may be collapsed for simplicity. Categories that do not apply (i.e. those with no patients) will not be shown.
Abbreviations: COPD: chronic obstructive pulmonary disease; COVID-19: coronavirus disease 2019.

Table S2: Causes of gastrointestinal sepsis*		
Characteristic	**Conservative oxygen therapy (n=xxxx)**	**Liberal oxygen therapy (n=xxxx)**
Gastrointestinal sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Infective oesophagitis	xxx (xx.x)	xxx (xx.x)
Infective enteritides	xxx (xx.x)	xxx (xx.x)
Necrotising enterocolitis	xxx (xx.x)	xxx (xx.x)
Appendicitis or appendiceal abscess	xxx (xx.x)	xxx (xx.x)
Diverticulitis or diverticular abscess	xxx (xx.x)	xxx (xx.x)
Infective colitis or proctocolitis	xxx (xx.x)	xxx (xx.x)
Infective hepatitis	xxx (xx.x)	xxx (xx.x)
Infective cholangitis	xxx (xx.x)	xxx (xx.x)
Hepatic abscess	xxx (xx.x)	xxx (xx.x)
Hydatid disease	xxx (xx.x)	xxx (xx.x)
Acute cholecystitis or empyema of gall bladder	xxx (xx.x)	xxx (xx.x)
Gangrenous gall bladder	xxx (xx.x)	xxx (xx.x)
Pancreatic abscess or infected pseudocyst	xxx (xx.x)	xxx (xx.x)
Infective pancreatitis	xxx (xx.x)	xxx (xx.x)
Primary peritonitis	xxx (xx.x)	xxx (xx.x)
Intra-peritoneal abscess (not pelvic)	xxx (xx.x)	xxx (xx.x)
CAPD related peritonitis	xxx (xx.x)	xxx (xx.x)
Pelvic infection or abscess	xxx (xx.x)	xxx (xx.x)
Retroperitoneal abscess or infection	xxx (xx.x)	xxx (xx.x)
Tuberculous peritonitis	xxx (xx.x)	xxx (xx.x)

* Where it is logical to combine categories, those with small numbers may be collapsed for simplicity. Categories that do not apply (i.e. those with no patients) will not be shown.
Abbreviations: CAPD: continuous ambulatory peritoneal dialysis.

Table S3: Causes of genitourinary sepsis*		
Characteristic	**Conservative oxygen therapy (n=xxxx)**	**Liberal oxygen therapy (n=xxxx)**
Genitourinary sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Pyelonephritis or pyonephrosis	xxx (xx.x)	xxx (xx.x)
Perinephric abscess	xxx (xx.x)	xxx (xx.x)
Cystitis, pyocystis or urethritis	xxx (xx.x)	xxx (xx.x)
Uterine cavity infection	xxx (xx.x)	xxx (xx.x)
Pelvic infection or abscess	xxx (xx.x)	xxx (xx.x)
Toxic shock syndrome	xxx (xx.x)	xxx (xx.x)
Tubo-ovarian abscess	xxx (xx.x)	xxx (xx.x)
Amnionitis	xxx (xx.x)	xxx (xx.x)
Infected retained products of conception	xxx (xx.x)	xxx (xx.x)
Septic abortion	xxx (xx.x)	xxx (xx.x)
Prostatitis	xxx (xx.x)	xxx (xx.x)
Testicular, prostatatic or penile abscess	xxx (xx.x)	xxx (xx.x)

* Where it is logical to combine categories, those with small numbers may be collapsed for simplicity. Categories that do not apply (i.e. those with no patients) will not be shown.

Table S4: Causes of musculoskeletal and skin sepsis*		
Characteristic	**Conservative oxygen therapy (n=xxxx)**	**Liberal oxygen therapy (n=xxxx)**
Musculoskeletal and skin sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Discitis	xxx (xx.x)	xxx (xx.x)
Spinal osteomyelitis or vertebral abscess	xxx (xx.x)	xxx (xx.x)
Osteomyelitis of the pelvis or long bones	xxx (xx.x)	xxx (xx.x)
Infective arthritis	xxx (xx.x)	xxx (xx.x)
Infected joint prosthesis	xxx (xx.x)	xxx (xx.x)
Myositis	xxx (xx.x)	xxx (xx.x)
Necrotising fasciitis	xxx (xx.x)	xxx (xx.x)
Rhabdomyolysis	xxx (xx.x)	xxx (xx.x)
Muscle or connective tissue abscess	xxx (xx.x)	xxx (xx.x)
Fournier's gangrene of abdominal wall	xxx (xx.x)	xxx (xx.x)
Fournier's gangrene of perineal tissues	xxx (xx.x)	xxx (xx.x)
Sternotomy related infection	xxx (xx.x)	xxx (xx.x)
Device related abdominal wall infection	xxx (xx.x)	xxx (xx.x)
Cutaneous cellulitis	xxx (xx.x)	xxx (xx.x)
Pressure injury, ulcers or sores	xxx (xx.x)	xxx (xx.x)

* Where it is logical to combine categories, those with small numbers may be collapsed for simplicity. Categories that do not apply (i.e. those with no patients) will not be shown.

Table S5: Other causes of sepsis*		
Characteristic	**Conservative oxygen therapy (n=xxxx)**	**Liberal oxygen therapy (n=xxxx)**
Infection present but not specified as the primary reason for ICU admission – n (%)	xxx (xx.x)	xxx (xx.x)
Cardiovascular system sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Viral or bacterial cardiomyopathy	xxx (xx.x)	xxx (xx.x)
Myocardial or septal abscess	xxx (xx.x)	xxx (xx.x)
Myocarditis	xxx (xx.x)	xxx (xx.x)
Non-valvular endocarditis	xxx (xx.x)	xxx (xx.x)
Infective pericarditis	xxx (xx.x)	xxx (xx.x)
Endocarditis, aortic root abscess, prosthetic heart valve infection, infected thoracic aortic prosthesis	xxx (xx.x)	xxx (xx.x)
Infected artificial pacemaker	xxx (xx.x)	xxx (xx.x)
Syphilitic aortitis	xxx (xx.x)	xxx (xx.x)
Infected thrombophlebitis of the great veins	xxx (xx.x)	xxx (xx.x)
Infected intravenous catheter in the great veins	xxx (xx.x)	xxx (xx.x)
Infected thrombophlebitis of the peripheral veins	xxx (xx.x)	xxx (xx.x)
Infected intravenous catheter in the peripheral veins	xxx (xx.x)	xxx (xx.x)
Infected arterio-venous shunt or fistula	xxx (xx.x)	xxx (xx.x)
Infected abdominal aortic prosthesis	xxx (xx.x)	xxx (xx.x)
Infected iliac prosthesis	xxx (xx.x)	xxx (xx.x)
Neurological system sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Meningitis, unspecified	xxx (xx.x)	xxx (xx.x)
Encephalitis	xxx (xx.x)	xxx (xx.x)
Intracranial abscess	xxx (xx.x)	xxx (xx.x)
Infected CSF shunt	xxx (xx.x)	xxx (xx.x)
Meningococcal meningitis	xxx (xx.x)	xxx (xx.x)
Bacterial meningitis, not meningococcal	xxx (xx.x)	xxx (xx.x)
Viral meningitis	xxx (xx.x)	xxx (xx.x)
Tuberculous meningitis	xxx (xx.x)	xxx (xx.x)
Epidural or subdural spinal infection	xxx (xx.x)	xxx (xx.x)
Poliomyelitis	xxx (xx.x)	xxx (xx.x)
Tetanus	xxx (xx.x)	xxx (xx.x)
Infective polyneuropathy	xxx (xx.x)	xxx (xx.x)
Leprosy	xxx (xx.x)	xxx (xx.x)
Botulism	xxx (xx.x)	xxx (xx.x)
Miscellaneous sepsis – n (%)	xxx (xx.x)	xxx (xx.x)
Leishmaniasis	xxx (xx.x)	xxx (xx.x)
Malaria	xxx (xx.x)	xxx (xx.x)
HIV	xxx (xx.x)	xxx (xx.x)
Septicaemia	xxx (xx.x)	xxx (xx.x)
Mononucleosis	xxx (xx.x)	xxx (xx.x)
Leptospirosis	xxx (xx.x)	xxx (xx.x)
Mediastinitis	xxx (xx.x)	xxx (xx.x)
Mandible, facial bones, dental or salivary infection	xxx (xx.x)	xxx (xx.x)
Orbital cellulitis	xxx (xx.x)	xxx (xx.x)
Mastoid infection	xxx (xx.x)	xxx (xx.x)

* Where it is logical to combine categories, those with small numbers may be collapsed for simplicity. Categories that do not apply (i.e. those with no patients) will not be shown.

FIGURES:

Figure 1: Participant flow diagram

Description: Participant flow diagram.

Figure 2A: Kaplan-Meier survival estimates of the probably 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.

Figure 2B: Forest plot for subgroup treatment effects on mortality: respiratory sepsis vs. gastrointestinal sepsis vs. genitourinary sepsis vs. other source of sepsis.

SUPPLEMENTAL FIGURES:

Figure S1A: Mean FiO_2 by treatment group

Description: Line graph with days 0 to 7 on the horizontal axis and FiO_2 on the vertical axis with mean daily FiO_2 shown by treatment group. The number of observations by group on each day will be indicated on the horizontal axis. The mean daily FiO_2 will be calculated from recordings of FiO_2 taken six hourly while the patient is invasively ventilated in the ICU up until day 7. Data points will be reported with corresponding standard error bars.

Figure S1B: Highest FiO_2 by treatment group

Description: Line graph with days 0 to 7 on the horizontal axis and FiO_2 on the vertical axis with the highest daily FiO_2 shown by treatment group. The number of observations by group on each day will be indicated on the horizontal axis. Highest FiO_2 will be recorded daily while the patient is invasively ventilated in ICU up until day 7. Data points will be reported with corresponding standard error bars.

Figure S1C: Lowest FiO_2 by treatment group

Description: Line graph with days 0 to 7 on the horizontal axis and FiO_2 on the vertical axis with the lowest daily FiO_2 shown by treatment group. The number of observations by group on each day will be indicated on the horizontal axis. Lowest FiO_2 will be recorded daily while the patient is invasively ventilated in ICU up until day 7. Data points will be reported with corresponding standard error bars.

Figure S2A: Mean daily PaO_2 by treatment group

Description: Line graph with days 0 to 7 on the horizontal axis and PaO_2 on the vertical axis with mean daily PaO_2 shown by treatment group. The number of observations by group on each day will be indicated on the horizontal axis. The mean daily PaO_2 will be calculated from recordings of PaO_2 taken six hourly while the patient is in the ICU up until day 7. Data points will be reported with corresponding standard error bars.

Figure S2B: Highest daily PaO_2 by treatment group

Description: Line graph with days 0 to 7 on the horizontal axis and PaO_2 on the vertical axis with the highest daily PaO_2 shown by treatment group. The number of observations by group on each day will be indicated on the horizontal axis. Highest PaO_2 will be recorded daily while the patient is in ICU up until day 7. Data points will be reported with corresponding standard error bars.

Figure S2C: Lowest PaO_2 by treatment group

Description: Line graph with days 0 to 7 on the horizontal axis and PaO_2 on the vertical axis with the lowest daily PaO_2 shown by treatment group. The number of observations by group on each day will be indicated on the horizontal axis. Lowest PaO_2 will be recorded daily while the patient is in ICU up until day 7. Data points will be reported with corresponding standard error bars.