

KOURAGE

Auxora for the Treatment of AKI and Modulation of Injurious
“Crosstalk” with the Lung: A Randomized Control Trial

NCT 06374797

KOURAGE Rationale

- A clinical phenotype with a high risk of mortality and morbidity are patients with Acute Kidney Injury (AKI) with associated acute hypoxemic respiratory failure (AHRF).
 - Patients with severe AKI who develop AHRF have documented hospital mortality rates of 50% or greater

ARDS and AKI: Worse Outcomes in the Presence of Stage 2 or 3

Table 3 Outcomes among patients with and without acute kidney injury

Outcomes	No AKI (113)	Stage I AKI (60)	Stage II AKI (66)	Stage III AKI (118)	<i>p</i>
Ventilator-free days to day 28, median (IQR), days	13 (0–20)	12 (0–18)	0 (0–14) ^a	0 (0–0) ^{a, b}	<0.001
Duration of mechanical ventilation, median (IQR), days	11 (6–18.3)	12 (8–18.3)	12 (7–20.8)	13 (6–22.8)	0.43
ICU length of stay, median (IQR), days	12 (6.8–17)	13 (9–22)	13 (6.3–20.8)	13 (7–25)	0.58
Hospital length of stay, median (IQR), days	16 (10–24.3)	17 (12.8–26)	20 (11.5–26.8)	19 (8–29)	0.82
ICU mortality (%)	32 (28.6)	17 (28.3)	32 (48.5)	72 (61) ^{a, b}	<0.001
Hospital mortality (%)	32 (28.6)	18 (30)	36 (54.5) ^a	73 (61.9) ^{a, b}	<0.001
Day 28 mortality (%)	29 (25.7)	19 (31.7)	32 (48.5) ^a	65 (55.1) ^{a, b}	<0.001
Day 90 mortality (%)	35 (31)	22 (36.7)	40 (60.6) ^a	73 (61.9) ^{a, b}	<0.001

AKI acute kidney injury, ICU intensive care unit, IQR interquartile range

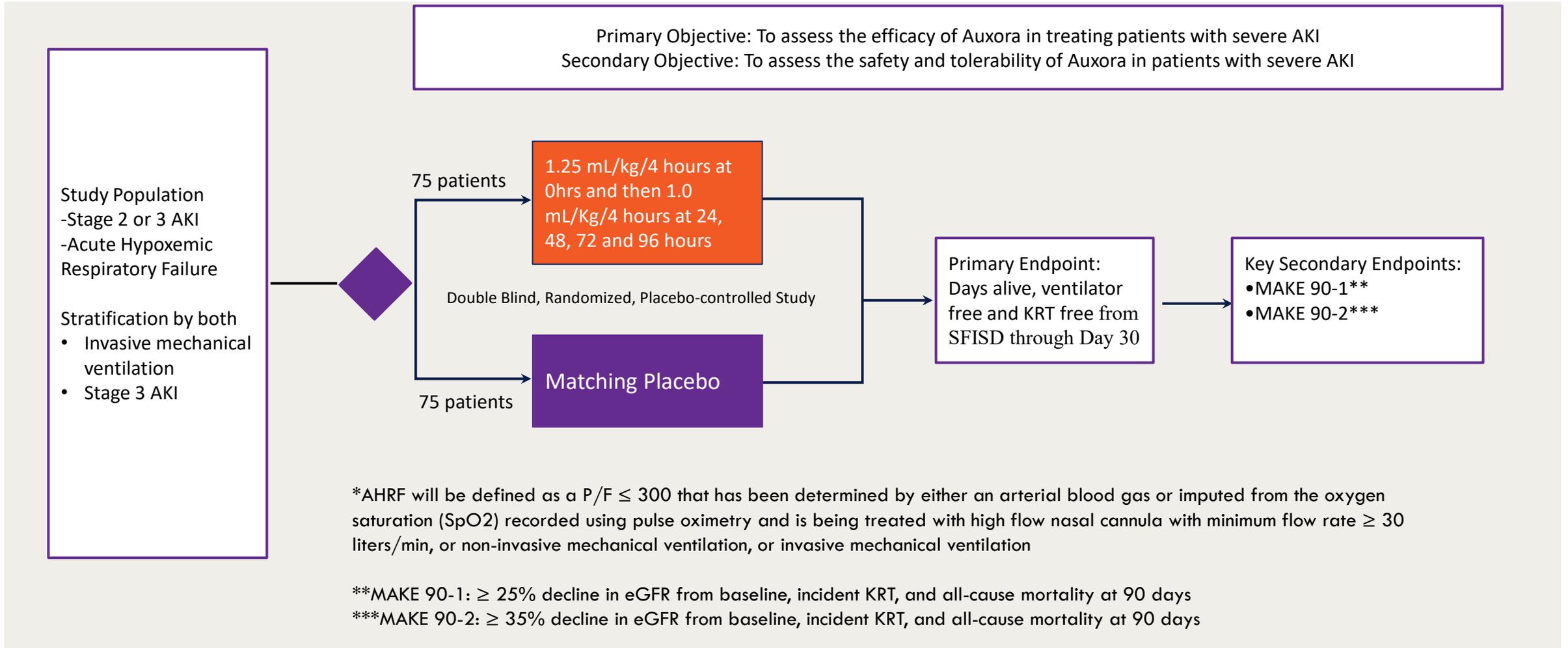
^a *p* < 0.05 when compared with patients without AKI

^b *p* < 0.05 when compared with patients with stage I AKI

KOURAGE Rationale: Results from the CARDEA Trial in Severe COVID-19

- Reported AKI Treatment-Emergent Adverse Events:
 - Auxora 7.1%
 - Placebo 11.4%
- CARDEA data analyzed post-hoc for efficacy of Auxora in 38 patients with AKI at screening
- 23 patients randomized to receive Auxora
 - 4/23 (17.4 %) died over 60 days
 - 13.8% mortality over 60 days for Auxora treated patients in study population as a whole
 - Death at Days 2, 3, 4, 13
- 15 patients randomized to receive Placebo
 - 7/15 (46.7%) died over 60 days
 - 20.6% mortality over 60 days for Placebo treated patients in study population as a whole
 - Death at Days 1, 4, 5, 7, 9, 9, 27
- RRR: 62.7% ARR: 29.3% in mortality with Auxora
- No increase in serious adverse events in patients with decreased eGFR treated with Auxora

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Inclusion Criteria

1. The patient is ≥ 18 years of age.
2. The patient has developed Stage 2 or Stage 3 AKI.
3. The patient has a documented $\text{PaO}_2/\text{FiO}_2$ (P/F) ≤ 300 in the prior 24 hours of informed consent, either imputed from SpO_2 or obtained from an arterial blood gas, that is not explained by cardiogenic pulmonary edema or volume overload.
4. The patient is being treated with either high flow nasal cannula with minimum flow rate ≥ 30 liters/min, or non-invasive mechanical ventilation, or invasive mechanical ventilation at time of randomization.

Select Exclusion Criteria

1. The patient has a do not intubate directive.
2. The patient has chronic lung disease that requires supplemental non-invasive oxygen as an outpatient or home mechanical ventilation.
Use of non-invasive mechanical ventilation to treat obstructive sleep apnea is not an exclusion.
3. The patient has been hospitalized* in the ICU for more than 10 days.
4. The patient has been receiving invasive mechanical ventilation for > 120 hours.
5. The patient is receiving ECMO.
6. The patient has started or is planned to start KRT before randomization.

Select Exclusion Criteria

7. The patient has a direct bilirubin level >3.0 mg/dL or both a direct bilirubin level ≥ 2.0 mg/dL and an INR ≥ 1.7 .
8. AKI is suspected to be secondary to:
 - a. renal artery or renal vein thrombosis;
 - b. hepato-renal syndrome;
 - c. cholesterol emboli syndrome;
 - d. acute glomerulonephritis;
 - e. vasculitis;
 - f. acute allergic interstitial nephritis;
 - g. intrarenal or extrarenal urinary tract obstruction;
 - h. use of immune checkpoint inhibitor.
9. The patient has a known history of an organ transplant

Endpoints for KOURAGE

- **Primary Endpoint**

- Days alive, ventilator free and Kidney Replacement Therapy (KRT) free from SFISD through Day 30

- **Secondary Endpoints**

- Major adverse kidney event (MAKE) 90-1: $\geq 25\%$ decline in eGFR from baseline, incident KRT, and all-cause mortality at 90 days
- MAKE 90-2: $\geq 35\%$ decline in eGFR from baseline, incident KRT, and all-cause mortality at 90 days
- Proportion of patients alive at Day 30
- Proportion of patients alive at Day 90
- Days alive and ventilator free from SFISD through Day 30
- Days alive and KRT free from SFISD through Day 30
- Proportion of patients recovered from AHRF through Day 30 as categorized by an 8-point ordinal scale
- Proportion of patients receiving KRT at Day 30
- Proportion of patients receiving KRT at Day 90