



# The Effects of Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitor on Long-Term Renal Outcomes in Post-Severe Acute Kidney Injury Survivors: Preliminary Analysis



## AKI & CRRT Conference

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### Introduction

- In Thailand, AKI in critical patients occurred about 52.9%, which 28.9% was stage 3 AKI.
- AKI survivors are increased risk of renal related and non-renal related complications
- The risk was also increased by staging of AKI.
- The renal recovery rate at hospital discharge was only 29%.

Short-term At 28 days	Incident	Overall (per 100 person-years)	Risk factors	MAKE <sub>365</sub>
Kidney recovery 29%	MAKE <sub>365</sub>	68.4	Non recovery	↑↑↑
Persistent AKI 39%	Incident CKD	82.8	Age	↑
Mortality 59%	CKD progression	42	Mixed ICU	↑
	All cause mortality	39.6	Malignancy	↑
	MAKE <sub>365</sub> 41%, Incident CKD 48%, CKD progression 28%, Death 26%			

No current medication has been established to improve outcomes in AKI survivors.

### Material and Methods

- Prospective, Multicenter, Double blinded Randomized Controlled Trial, involving 3 tertiary hospitals
  - King Chulalongkorn Memorial Hospital, Bangkok, Thailand
  - Central Chest Institute of Thailand, Bangkok, Thailand
  - Buddhachinaraj Hospital, Phitsanulok, Thailand

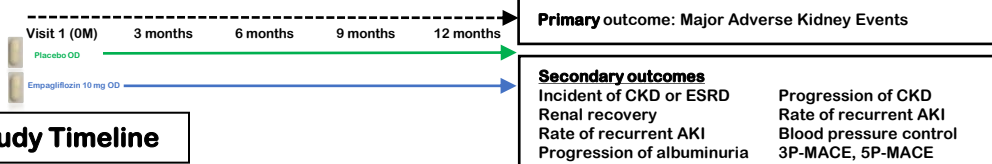
#### Inclusion Criteria

- Severe AKI (AKI stage 2-3 by KDIGO 2012 classifications)
- eGFR  $\geq 20$  ml/min/1.73m<sup>2</sup> by CKD-EPI creatinine equation before starting interventions
- Stable SCr or eGFR (change  $\leq 25\%$  compared to baseline)

#### Exclusion Criteria

- End stage kidney disease
- Kidney transplantation recipients
- Moribund patients whose survival  $< 1$  month
- Drug allergy or contraindicated to SGLT2i
- Diabetes mellitus type 1, Pregnancy
- History of ketoacidosis
- Previous use of SGLT2 inhibitors

#### Enrollment Randomization



#### Study Timeline

### Results

- Both groups were still blinded during the preliminary analysis. Out of 188 enrolled patients, only 99 patients (52 in group A and 47 in group B) completed 1 year follow up.
- 60% of the patients were male in both groups, 50% of them had diabetes mellitus and 25% had chronic kidney disease. Median baseline eGFR was 75 and 72 ml/min/1.73 m<sup>2</sup> in group A and B respectively.
- At 12-month follow up, 21 patients in group A and 27 patients in group B developed MAKE<sub>365</sub> (40.0% vs. 57.0%, HR 1.55, 95% CI 0.87-2.75),  $p = 0.133$ .
- Death occurred in 15 percent and 6 percent in group A and B (HR 0.39, 95% CI 0.10-1.48)  $p = 0.167$ . 44 patients in each group had persistent renal dysfunction (85% vs. 94%,  $p = 0.155$ )

Table 1: Demographic Data

Characteristics	A (N = 93)	B (N = 92)	p-value
Age (years)	63.5 $\pm$ 15.1	64.2 $\pm$ 13.1	0.724
Male	55 (59.1%)	52 (56.5%)	0.654
Height	161.5 $\pm$ 9.2	158.3 $\pm$ 19.9	0.501
Body weight	62.9 $\pm$ 16.6	62.4 $\pm$ 17.3	0.194
Underlying disease			
Hypertension	76 (81.7%)	82 (89.1%)	0.158
Diabetes	47 (50.5%)	48 (52.2%)	0.824
Ischemic heart disease	33 (35.5%)	36 (39.1%)	0.608
Chronic Kidney disease	49 (52.7%)	29 (31.5%)	0.305
Baseline Medications			
ACEI/ARB	30 (32.3%)	31 (33.7%)	0.438
Beta blocker	43 (46.2%)	45 (48.9%)	0.611
Diuretics	34 (36.6%)	33 (35.9%)	0.942
Insulin	18 (19.4%)	17 (18.5%)	0.936
Anticoagulant	18 (19.4%)	23 (25.0%)	0.357
Antiplatelet	36 (38.7%)	38 (41.3%)	0.628
Statin	62 (66.7%)	57 (62.0%)	0.637
Med reconciliation	88 (94.6%)	87 (94.6%)	0.503
AKI stage 3	65 (69.9%)	69 (75.0%)	0.437
Renal replacement therapy	19 (20.4%)	27 (29.3%)	0.162

Table 1: Demographic Data (con't)

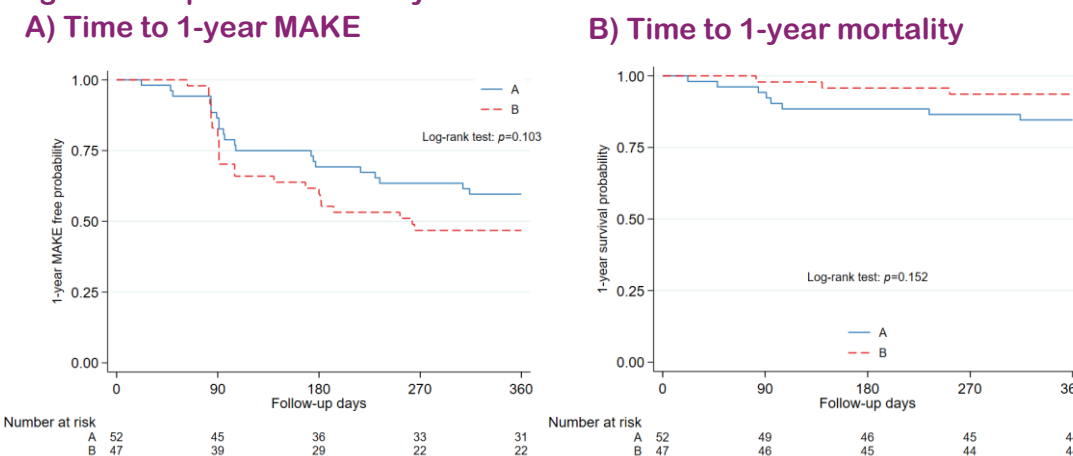
Causes of AKI			
Ischemic/Prerenal	49 (52.7%)	49 (53.3%)	0.938
Sepsis	22 (23.7%)	22 (23.9%)	0.967
Nephrotoxic	24 (25.8%)	26 (28.3%)	0.707
Baseline Kidney function			
Creatinine	1.0 (0.60-2.28)	1.04 (0.57-2.6)	0.792
eGFR	75.0 (23.7-131.3)	72.1 (24.0-109.0)	0.321
Kidney function at hospital discharge			
Creatinine	1.38 (0.44-5.40)	1.51 (0.48-7.25)	0.293
eGFR	48.0 (9.89-127.1)	39.6 (6.98-125.9)	0.478

Table 2: Outcomes

	A (N= 52)	B (N=47)	p-value
1-year MAKE, n (%)	21 (40)	27 (57)	0.090
Hospital 1	8/11 (73)	8/10 (80)	
Hospital 2	6/18 (33)	10/17 (59)	
Hospital 3	7/23 (30)	9/20 (45)	
1-year MAKE category, n (%)			
Dead	8 (15)	3 (6)	0.155
Dialysis dependent	0 (0)	0 (0)	-
Persistent renal dysfunction	44 (85)	44 (94)	0.155
1-year MAKE incidence (95% CI), per 1000 person-year	540 (334, 826)	876 (577, 1000†)	
Hospital 1	1000† (697, 1000†)	1000† (646, 1000†)	
Hospital 2	410 (151, 893)	894 (428, 1000†)	
Hospital 3	363 (146, 748)	629 (288, 1000†)	
1-year MAKE Hazard ratio (95% CI) *	Reference	1.59 (0.90, 2.82)	0.109
1-year MAKE Hazard ratio (95% CI) considering for cluster effects of hospitals**	Reference	1.55 (0.87, 2.75)	0.133
1-year mortality rate (95% CI), per 1000 person-year	171 (74, 337)	66 (14, 194)	
1-year mortality hazard ratio (95% CI)*	Reference	0.39 (0.10, 1.48)	0.167
1-year mortality hazard ratio (95% CI) considering for cluster effects of hospitals**	Reference	0.39 (0.10, 1.46)	0.161

\* Cox proportional Hazard regression model; \*\* Multilevel mixed-effects parametric survival models  
 † The incidence rate per 1000 person-year which exceeded 1000 was simplified as 1000.

Figure 1: Kaplan Meier on 1-year outcomes



### Discussion

- Higher MAKE rate compared to previous study as we included only severe AKI patients
- High MAKE<sub>365</sub> emphasizes need for intervention in this high risk population.
- SGLT2i is safe to use in Post AKI setting with low adverse events.

#### Strengths

- First multicenter double blinded randomized controlled trial, focused on effects of SGLT2i in post AKI setting

#### Limitations

- Slow recruitment rates due to Covid era.
- Concomitant treatment with SGLT2i from other specialists, especially cardiologists.

### Conclusions

In our preliminary result, there was no clear difference in renal and non-renal outcomes between groups.



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