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Challenge Your Thinking

CKD Identifies Treatment-Responsive Subgroups in the Phase 3 Trial of RBT-1 in Cardiac Surgery

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protect

INTRODUCTION

- Chronic kidney disease (CKD) is associated with poor postoperative outcomes and a higher risk of mortality following cardiac surgery
- RBT-1, a combination of stannic protoporfin (SnPP) and iron sucrose (FeS), is a preconditioning agent that activates anti-inflammatory and antioxidant pathways when administered prior to surgery
- PROTECT, a Phase 3 trial, evaluated the effect of RBT-1 on postoperative complications in patients undergoing on-pump cardiac surgery
- The trial was overall neutral and failed to show benefit in the overall population
- We hypothesized that insufficient enrichment for operative risk may have diluted the treatment effect

METHODS

- Randomized, double blind, placebo-controlled trial in patients undergoing non-emergent cardiac surgery
- Primary endpoint was a hierarchical composite of death, AKI receiving dialysis, hospital readmission, and ICU length of stay, assessed using the win ratio method (WR; >1 favors RBT-1)
- Post-hoc analyses stratified participants by CKD status (eGFR ≤60 vs. >60 mL/min/1.73m²) and perioperative outcomes as predicted by the Society of Thoracic Surgeons (STS) Short-term/Operative Risk Calculator

RESULTS

Group / subgroup (N = 418: RBT-1 vs Pbo)	Win ratio (WR)	WR (95% CI)	p–value
Overall Study Population (n= 214 vs 204)		0.87 (0.66–1.15)	0.33
CKD and/or STS High risk threshold (n= 39 vs 38)		1.55 (0.85–2.84)	0.15
CKD and STS High risk (n= 19 vs 19)		2.09 (0.88–4.95)	0.09
CKD and not STS High risk (n= 20 vs 19)		1.11 (0.49–2.52)	0.80
STS morbidity/mortality ≥15% (n= 37 vs 30)		1.62 (0.88–2.99)	0.13
CKD (n= 15 vs 12)		2.62 (0.96–7.10)	0.06
Non–CKD (n= 22 vs 18)		1.17 (0.54–2.54)	0.69
STS operative mortality ≥4% (n= 26 vs 23)		1.43 (0.72–2.86)	0.31
CKD (n= 11 vs 10)		2.39 (0.81–7.02)	0.11
Non–CKD (n= 15 vs 13)		0.94 (0.39–2.25)	0.89
STS prolonged ventilation ≥10% (n= 33 vs 24)		1.88 (0.94–3.71)	0.07
CKD (n= 11 vs 10)		2.85 (0.91–8.97)	0.07
Non–CKD (n= 22 vs 14)		1.39 (0.61–3.20)	0.43
STS renal failure ≥2.8% (n= 40 vs 32)		1.44 (0.87–2.40)	0.10
CKD (n= 20 vs 18)		2.07 (0.87–4.95)	0.10
Non–CKD (n= 20 vs 14)		1.05 (0.46–2.43)	0.90

CONCLUSIONS

- Post hoc analyses in higher-risk subgroups (subjects with CKD or multiple STS risk thresholds) showed directionally consistent win ratio estimates favoring RBT-1
- A majority (~70%) of enrolled patients met neither CKD nor STS high-risk criteria, consistent with lower-than-anticipated event rates in PROTECT
- A prospective trial with enrichment for CKD is warranted to confirm these findings