GUARD THERAPEUTICS

21-ROS-05 (AKITA) Top-line results

Investor Webcast & Teleconference

September 19, 2023

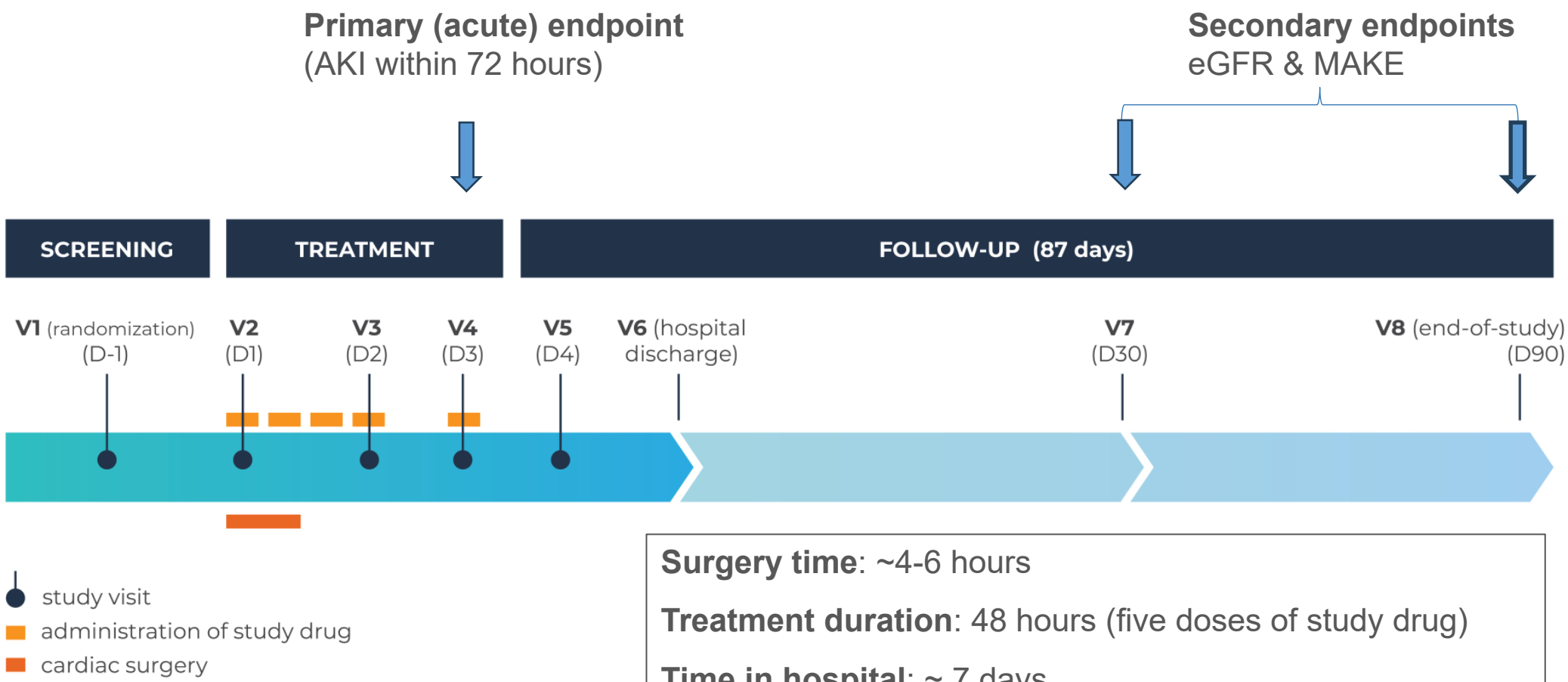
GUARD THERAPEUTICS – INTRODUCTION

- Clinical stage biotechnology company (Stockholm, Sweden)
- Focus on kidney diseases (acute & chronic)
- Lead investigational drug RMC-035
  - US FDA Fast Track Designation in open-heart surgery
    - For prevention of death, dialysis, or an irreversible loss of kidney function
  - Phase 2 development in open-heart surgery (AKITA study)
  - Phase 1b study completed in kidney transplantation

PHASE 2 AKITA STUDY – MAIN OBJECTIVES

- Evaluate the efficacy & safety of RMC-035 in open-heart surgery
- Establish relevant efficacy signal(s) to guide further development
  - Not intended for regulatory approval
  - Multiple endpoints critical for decision on continued development
    - Acute endpoints – short-term prognostic markers for “hard” clinical outcomes
    - Chronic endpoints – “hard” outcomes to be confirmed in Phase 3 (to support marketing approval)
      - Highest clinical relevance (“treat the disease, not the biomarker”)
- In this indication, no single Phase 2 endpoint captures all relevant treatment effects

AKITA STUDY – OVERVIEW & FLOWCHART



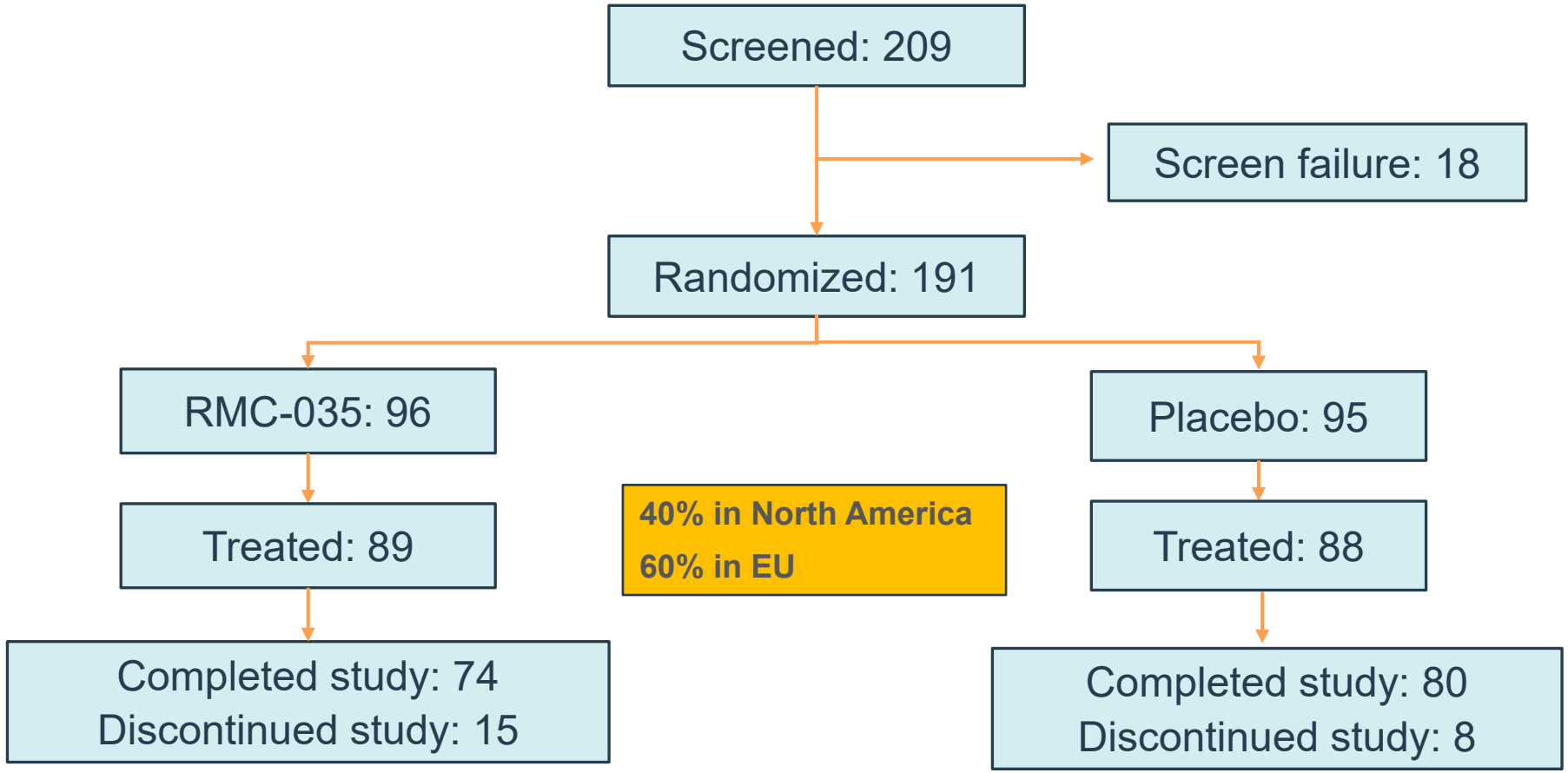
Surgery time: ~4-6 hours

Treatment duration: 48 hours (five doses of study drug)

Time in hospital: ~ 7 days

Follow-up time: up to 90 days after surgery

SUBJECT DISPOSITION



Source: Table 14.1.1.1

BASELINE CHARACTERISTICS ARE WELL BALANCED

	RMC-035 (N=89)	Placebo (N=88)
Age (years)	70.2 (8.5)	70.5 (8.1)
Male	70 (78.7%)	69 (78.4%)
Female	19 (21.3%)	19 (21.6%)
Height (cm)	169.8 (8.9)	171.3 (9.0)
Weight (kg)	83.3 (18.1)	86.3 (20.5)
eGFR (mL/min/1.73m^2)	75.6 (18.1)	77.4 (18.2)
Subgroup ≥ 60 mL/min/1.73m^2	55 (61.8 %)	57 (64.8 %)
Subgroup < 60 mL/min/1.73m^2	34 (38.2 %)	31 (35.2 %)

Start dose: 1.30 mg/kg

Start dose: 0.65 mg/kg

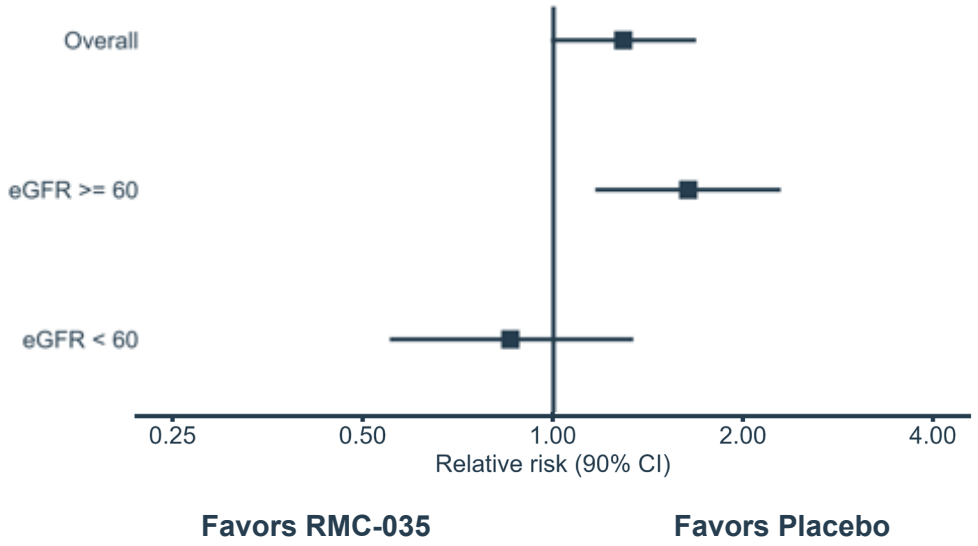
Table shows frequency (proportion) for categorical variables and mean (Standard Deviation, SD) for continuous variables.
eGFR, estimated glomerular filtration rate

Source: Tables 14.1.3, 14.1.4.

PRIMARY ENDPOINT (AKI WITHIN 72 HOURS AFTER SURGERY)

STRONG TREND FAVORING PLACEBO

	RMC-035 (N=89)	Placebo (N=88)	Relative Risk (90% CI)
Overall AKI rate	**45 (50.6%)**	**35 (39.8%)**	**1.30 (0.99, 1.71) p=0.12**
eGFR ≥60	31 (56.4%)	20 (35.1%)	1.66 (1.17, 2.35)
eGFR <60	14 (41.2%)	15 (48.4%)	0.85 (0.54, 1.35)



AKI definition:
Serum creatinine increase of ≥ 50%, or absolute increase of ≥0.3 mg/dL

Table shows frequency (proportion) for AKI incidence. eGFR, estimated glomerular filtration rate.

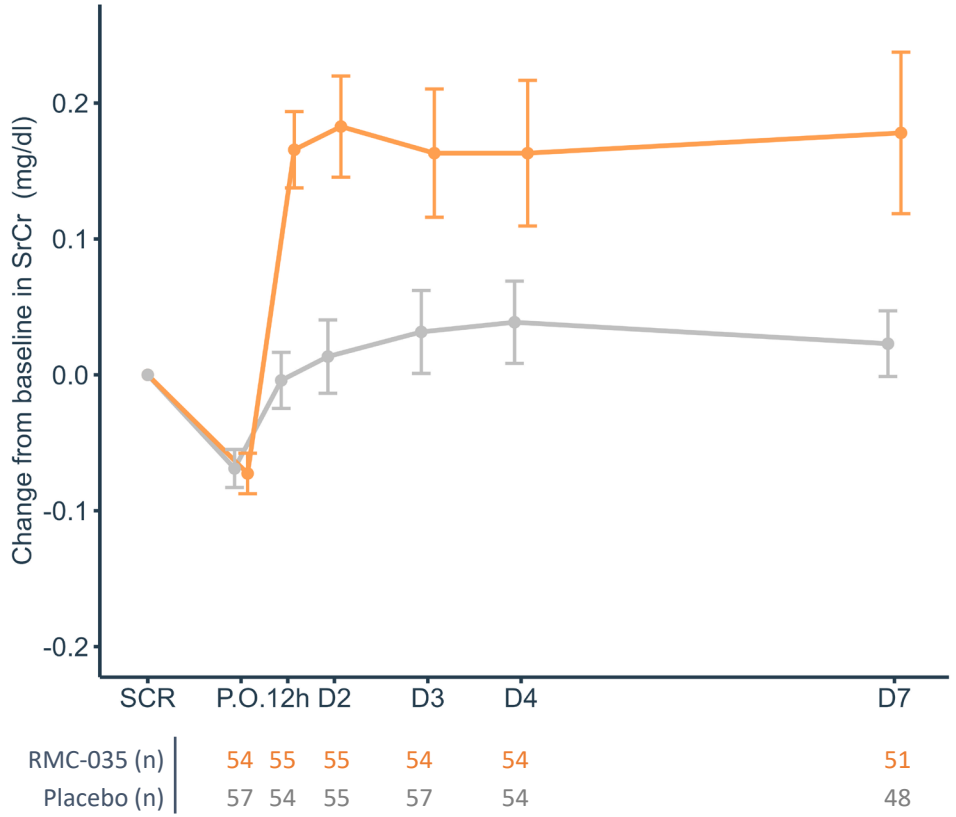
Source: Table 14.2.1.1.1 to Table 14.2.1.1.5.

SERUM CREATININE: CHANGE FROM BASELINE TO DAY 7

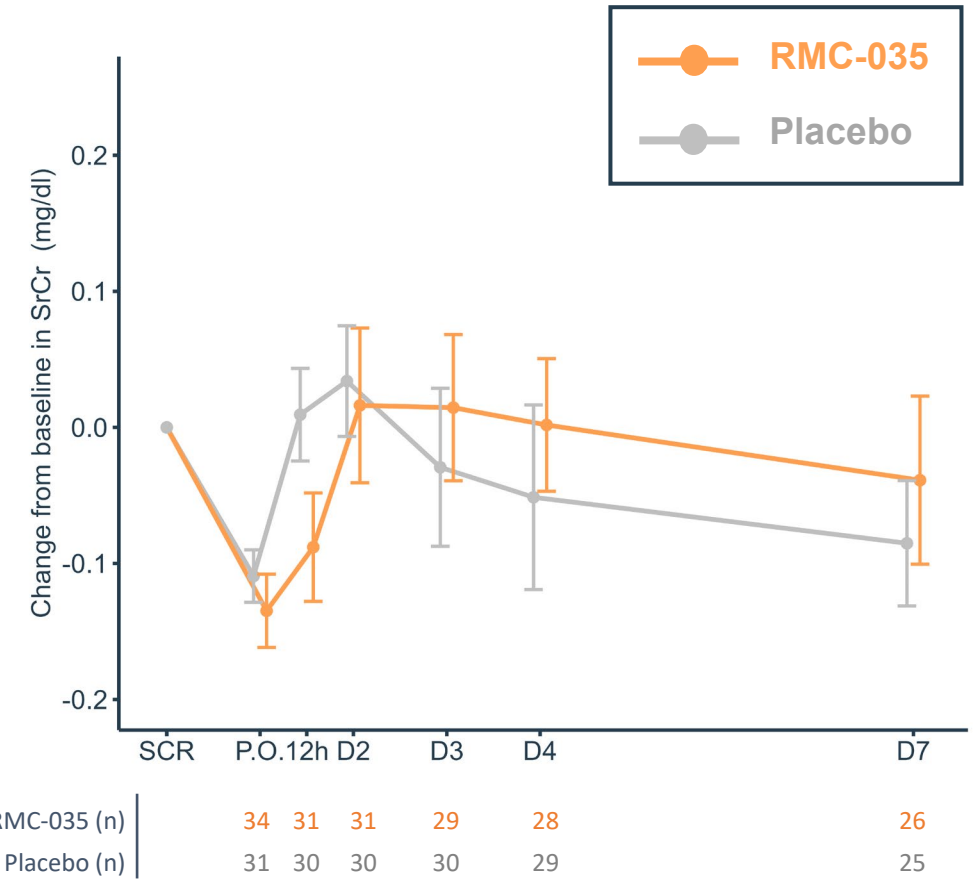
ACUTE CREATININE RISE DRIVEN BY HIGHER RMC-035 START DOSE

eGFR ≥ 60 mL/min/1.73m²

Acute creatinine increase (even when reversible & harmless) → triggering "AKI" by definition



eGFR < 60 mL/min/1.73m²



Error bars indicate mean +/- Standard Error (SE); P.O, pre-operative (before surgery); SCR, Screening; SrCr, serum creatinine

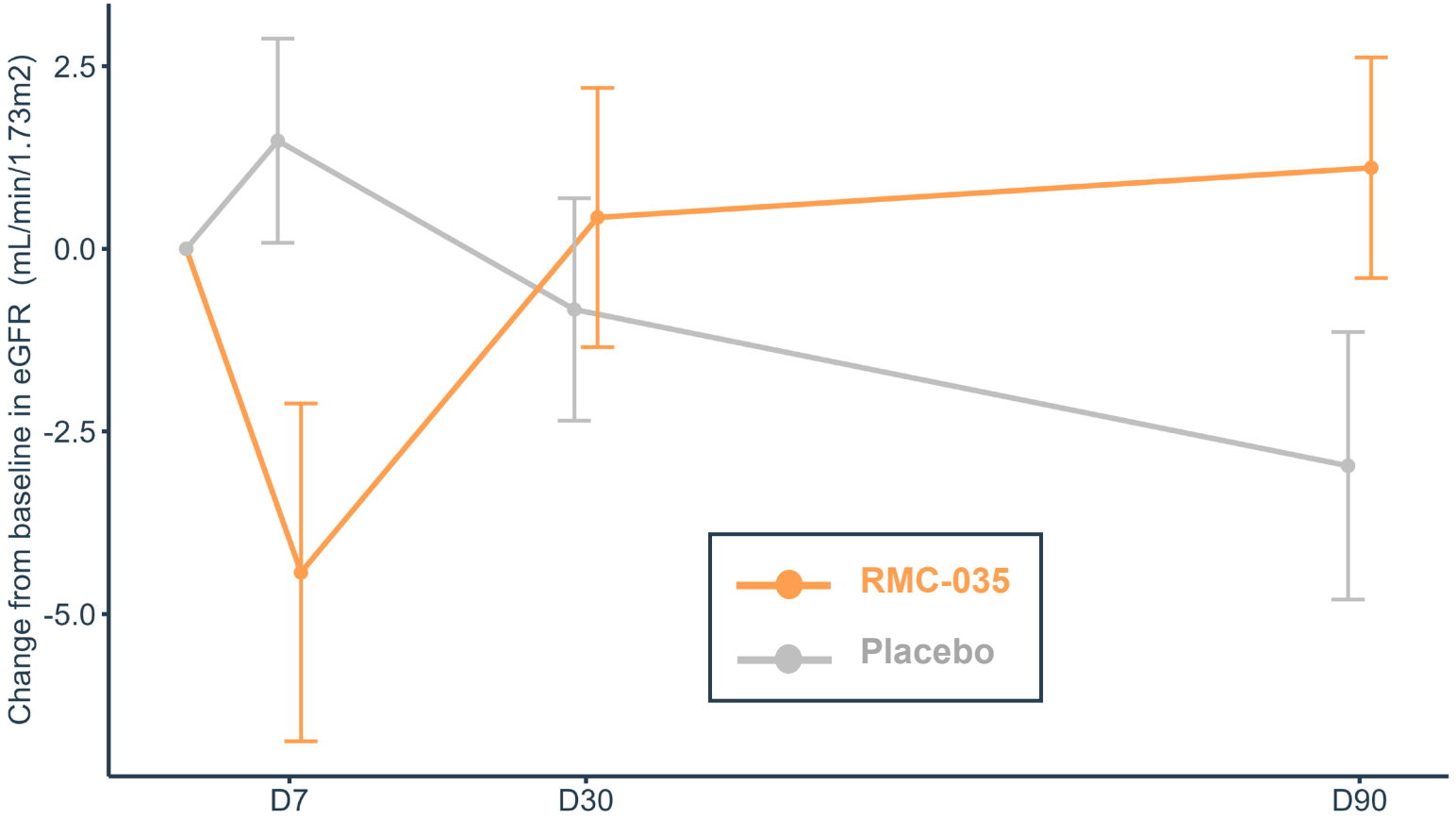
Source: Post-hoc analysis of pre-specified endpoint and eGFR subgroup

LONG-TERM EFFECTS ON “HARD” CLINICAL ENDPOINTS (PRE-SPECIFIED SECONDARY ENDPOINTS)

RENAL FUNCTION (eGFR) & MAJOR ADVERSE KIDNEY EVENTS (MAKE)

CHANGE FROM BASELINE IN RENAL FUNCTION (eGFR)

CLINICALLY RELEVANT & SIGNIFICANT IMPROVEMENT OF LONG-TERM KIDNEY FUNCTION WITH RMC-035



	D7	D30	D90
RMC-035 (n)	77	68	64
Placebo (n)	73	69	69

eGFR benefit at Day 90:

Measured	MMRM model
4.1 mL/min	4.3 mL/min **p=0.063***

Pre-defined alpha level was 0.1.
P-values < 0.1 are statistically significant.

Error bars indicate mean +/- Standard Error (SE); eGFR, estimated glomerular filtration rate; MMRM, Mixed Model of Repeated Measures

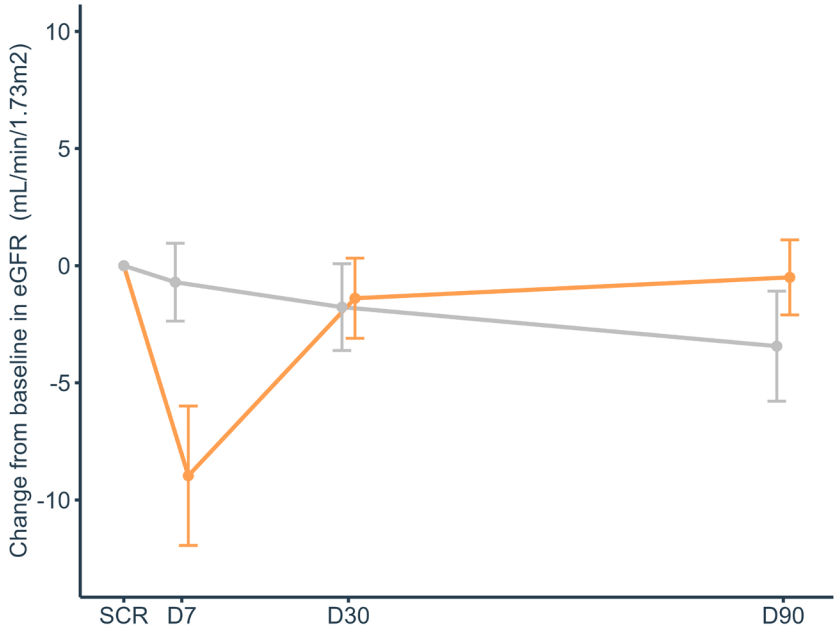
Source: Table 14.2.3.3.1.

CHANGE FROM BASELINE IN RENAL FUNCTION (eGFR)

IMPROVEMENT OF LONG-TERM KIDNEY FUNCTION EVEN STRONGER IN SUBGROUP WITH LOWER RMC-035 START DOSE

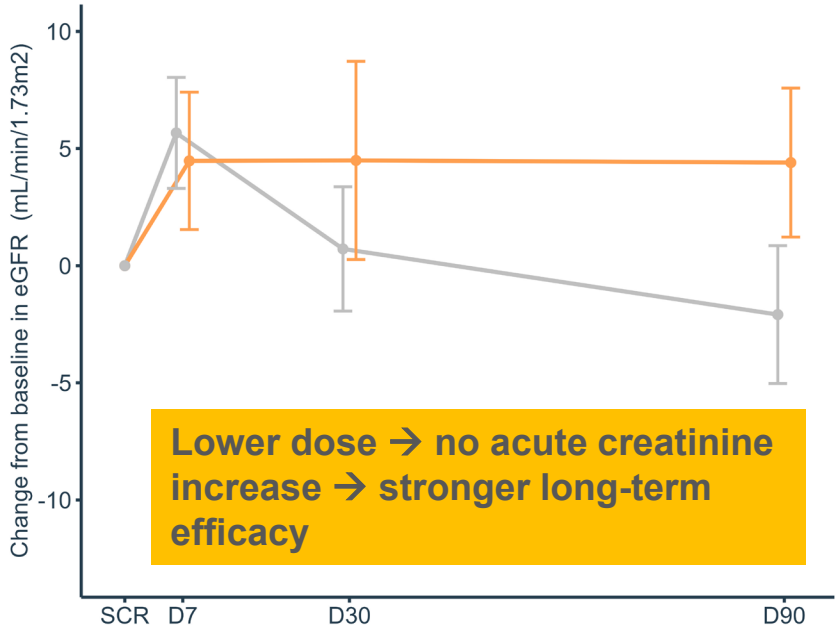
eGFR subgroups pre-specified based on different start doses and risk for kidney injury

eGFR ≥ 60 mL/min/1.73m^2



RMC-035 (n)	51	47	43
Placebo (n)	48	43	45

eGFR < 60 mL/min/1.73m^2



RMC-035 (n)	26	21	21
Placebo (n)	25	26	24

Lower dose → no acute creatinine increase → stronger long-term efficacy

eGFR benefit at Day 90:

Subgroup	Measured	MMRM model
eGFR ≥ 60	2.9 mL/min	2.3 mL/min p=0.41
eGFR < 60	6.5 mL/min	7.9 mL/min **p=0.051***

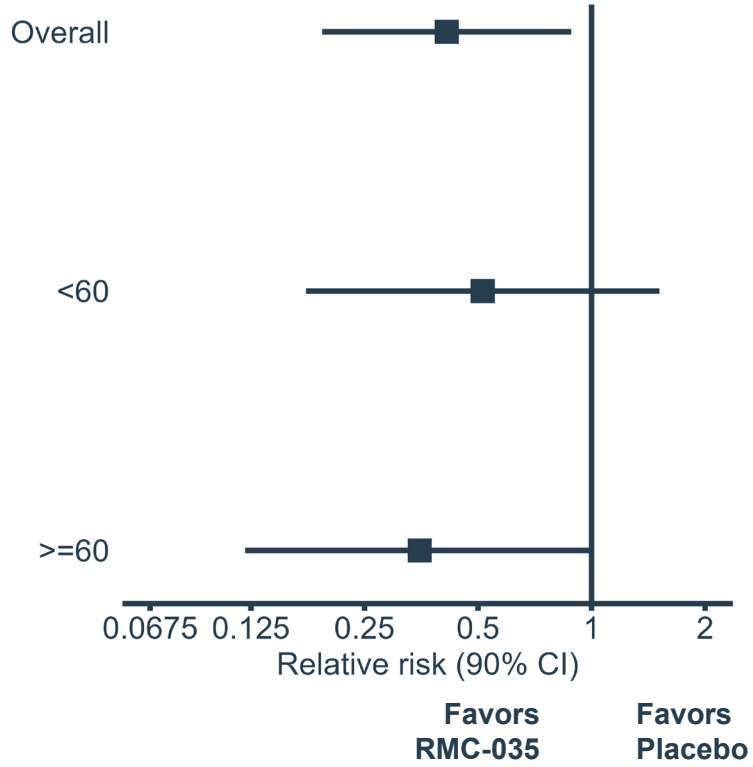
Pre-defined alpha level was 0.1.
P-values < 0.1 are statistically significant.

Source: Table 14.2.3.3.1 Error bars indicate mean +/- Standard Error; MMRM, Mixed Model of Repeated Measures

MAJOR ADVERSE KIDNEY EVENTS AT DAY 90 (MAKE 90)

CLINICALLY RELEVANT & SIGNIFICANT REDUCTION OF MAKE 90 (EXPECTED PRIMARY PHASE 3 ENDPOINT)

	RMC-035 (N=89)	Placebo (N=88)
Number (%) of Subjects with MAKE at Day 90	6 (6.7%)	14 (15.9%)
Death through Day 90	4	4
Dialysis through Day 90	3	2
≥25% eGFR† reduction at Day 90	**3**	**10**
Relative Risk (90% CI)	0.41 (0.19, 0.88) **p=0.047***	



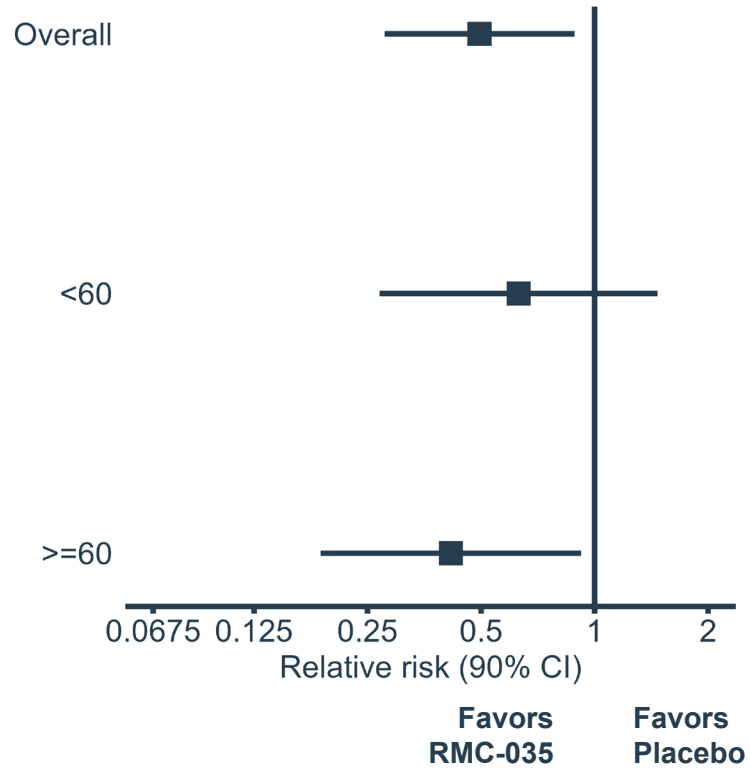
CI, confidence interval
MAKE, Major Adverse Kidney Events, †eGFR calculated using CKD-EPI equation with serum creatinine

Source: Table 14.2.3.9.1

MAKE 90 – SENSITIVITY ANALYSIS WITH DIFFERENT METHOD TO DETERMINE eGFR

CONFIRMS ROBUST EFFICACY SIGNAL ON REGULATORY ENDPOINT

	RMC-035 (N=89)	Placebo (N=88)
Number (%) of Subjects with MAKE at Day 90	10 (11.2%)	20 (22.7%)
Death through Day 90	4	4
Dialysis through Day 90	3	2
≥25% eGFR† reduction at Day 90	**7**	**15**
Relative Risk (90% CI)	0.50 (0.28, 0.88) **p=0.041***	



CI, confidence interval
MAKE, Major Adverse Kidney Events, †eGFR calculated using CKD-EPI equation with serum creatinine & cystatin C

Source: Table 14.2.3.9.3

SAFETY – TREATMENT-EMERGENT ADVERSE EVENTS

SAFETY PROFILE CONSISTENT WITH EXPECTED ADVERSE EVENTS IN THIS PATIENT POPULATION

	RMC-035 (N=89)	Placebo (N=88)
	n (%)	n (%)
TEAE	76 (85.4)	66 (75.0)
TEAE leading to discontinuation of study drug	5 (5.6)	5 (5.7)
Serious TEAE	20 (22.5)	15 (17.0)
TEAE leading to death	1 (1.1)	2 (2.3)
TEAE suggestive of IRRs on days of treatment	32 (36.0)	5 (5.7)

TEAE = Treatment-emergent adverse event, defined as onset of event within 72 hours after last treatment; IRR = infusion-related reactions

Source: Table 14.3.1.2.1

KEY FINDINGS – SUMMARY

- Primary (short-term) endpoint AKI was not met. However,
  - RMC-035 dose too high (eGFR subgroup ≥ 60), triggering “AKI” by definition
  - Too high dose invalidates purpose of AKI as primary endpoint
    (i.e., to predict MAKE reduction in Phase 3)
- Strong & consistent efficacy signals on pre-specified secondary endpoints reflecting “hard” clinical outcomes
  - Significant & clinically relevant eGFR improvement on Day 90
  - Significant & clinically relevant reduction of MAKE on Day 90
    (i.e., primary endpoint in a future Phase 3 study as required by regulatory agencies)
- Efficacy & safety profiles support further development

CONCLUSIONS & PATH FORWARD

- Robust evidence that RMC-035 prevents an irreversible loss of kidney function
  - In line with US Fast Track Designation for RMC-035
- Clinically relevant effects shown on “hard outcomes” (eGFR, MAKE)
- **Decision to proceed to late phase development based on AKITA results:**
  - Expected Phase 3 primary endpoint (MAKE on Day 90) was met
  - Significant & clinically relevant improvement on renal function on Day 90
  - Consistency between continuous (eGFR) and binary (MAKE) kidney endpoints
  - eGFR difference shown in AKITA predicts success in Phase 3 with MAKE 90 endpoint
- More details on clinical path forward will be communicated shortly