Supplementary Online Content

Boyle AJ, Schultz C, Selvanayagam JB, et al. Calcium/calmodulin-dependent protein kinase II delta inhibition and ventricular remodeling after myocardial infarction: a randomized clinical trial. *JAMA Cardiol*. Published online April 14, 2021. doi:10.1001/jamacardio.2021.0676

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Exclusion Criteria

A subject who met any of the following criteria was not eligible for participation in this study:
1. Pregnant or breastfeeding females;

2. Known cardiomyopathy or heart failure prior to MI;

3. Cardiogenic shock and/or systolic blood pressure < 85 mmHg at screening;

4. Clinical history of ejection fraction ≤ 45% prior to MI, or multiple prior MIs;

5. Daily use of non-steroidal anti-inflammatory drugs (NSAIDs) and/or cyclooxygenase-2 (COX-2) inhibitors in the past month;

6. Prior coronary artery bypass graft to culprit vessel;

7. Presence of device/hardware incompatible with MRI imaging;

8. Estimated glomerular filtration rate < 30 mL/min;

9. Liver function tests 3 x ULN due to non-cardiac disease;

10. Receipt of any investigational research agent within 30 days or 5 half-lives (whichever was longer) prior to the first dose of IP;

11. History of severe or life-threatening drug allergy and/or known drug hypersensitivity;

12. Current malignancy or previous malignancy that was likely to recur during the period of the study (with the exception of a past history of basal or squamous cell carcinomas);

13. Human immunodeficiency virus, hepatitis B or hepatitis C;

14. Other than the current STEMI, history of or current clinically significant gastrointestinal, hepatic, renal, cardiovascular, respiratory, endocrine, oncological, immunodeficiency, neurological, metabolic, haematological, autoimmune or psychological disorder that, in the investigator's opinion, would compromise subject safety or protocol compliance;

15. Clinical signs of active infection and/or a temperature of >38.0°C at the time of screening.

eTable 1. Major Adverse Cardiac and Cerebrovascular Events (MACCE)

	NP202 (N=66)		Placebo (N=71)		P value
	n (%)	[95% CI]	n (%)	[95% CI]	
Any MACCE event	5 (7.6%)	[2.5, 16.8]	7 (9.9%)	[0.9, 11.9]	NS
Type of MACCE					
- Non-fatal MI	0	[0.0, 5.4]	0	[0.0, 5.1]	NS
- Non-fatal Stroke	0	[0.0, 5.4]	0	[0.0, 5.1]	NS
- Cardiac hospitalization due to heart failure	3 (4.5%)	[0.9, 12.7]	4 (5.6%)	[0.0, 5.1]	NS
- Cardiovascular death	2 (3.0%)	[0.4, 10.5]	2 (2.8%)	[0.3, 9.8]	NS

eTable 2. ECG Findings

Visit	NP202 (N=66) n (%)	Placebo (N=71) n (%)	Overall (N=137) n (%)
Screening: n	60	67	127
Normal	1 (1.7%)	2 (3.0%)	3 (2.4%)
Abnormal, not-clinically significant	45 (75.0%)	45 (67.2%)	90 (70.9%)
Abnormal, clinically significant	14 (23.3%)	20 (29.9%)	34 (26.8%)
Visit 1 (Day 1): n	34	44	78
Normal	2 (5.9%)	1 (2.3%)	3 (3.8%)
Abnormal, not-clinically significant	28 (82.4%)	41 (93.2%)	69 (88.5%)
Abnormal, clinically significant	4 (11.8%)	2 (4.5%)	6 (7.7%)
Visit 2 (Day 14): n	55	62	117
Normal	5 (9.1%)	4 (6.5%)	9 (7.7%)
Abnormal, not-clinically significant	47 (85.5%)	57 (91.9%)	104 (88.9%)
Abnormal, clinically significant	3 (5.5%)	1 (1.6%)	4 (3.4%)
Visit 3 (Day 30): n	52	66	118
Normal	6 (11.5%)	4 (6.1%)	10 (8.5%)
Abnormal, not-clinically significant	44 (84.6%)	62 (93.9%)	106 (89.8%)
Abnormal, clinically significant	2 (3.8%)	0	2 (1.7%)
Visit 4 (Day 60): n	51	63	114
Normal	8 (15.7%)	7 (11.1%)	15 (13.2%)
Abnormal, not-clinically significant	41 (80.4%)	56 (88.9%)	97 (85.1%)
Abnormal, clinically significant	2 (3.9%)	0	2 (1.8%)
Visit 5 (Day 90): n	50	62	112
Normal	11 (22.0%)	5 (8.1%)	16 (14.3%)
Abnormal, not-clinically significant	37 (74.0%)	55 (88.7%)	92 (82.1%)
Abnormal, clinically significant	2 (4.0%)	2 (3.2%)	4 (3.6%)
Early Withdrawal: n	2	3	5
Normal	0	1 (33.3%)	1 (20.0%)
Abnormal, not-clinically significant	2 (100%)	2 (66.7%)	4 (80.0%)
Abnormal, clinically significant	0	0	0
End of Study (Day 120): n	50	61	111
Normal	14 (28.0%)	7 (11.5%)	21 (18.9%)
Abnormal, not-clinically significant	35 (70.0%)	53 (86.9%)	88 (79.3%)
Abnormal, clinically significant	1 (2.0%)	1 (1.6%)	2 (1.8%)

Data is presented as n (%) where n is the number of subjects, % is the percentage of subjects within a treatment group.

eTable 3. Adverse Events Associated With Changes to ECG Parameters

Preferred Term	NP202 (N=66) n (%)	Placebo (N=71) n (%)	Overall (N=137) n (%)
Palpitations	2 (3.0%)	1 (1.4%)	3 (2.2%)
Arrhythmia	0	2 (2.8%)	2 (1.5%)
Electrocardiogram abnormal	1 (1.5%)	1 (1.4%)	2 (1.5%)
Bradycardia	2 (3.0%)	0	2 (1.5%)
Ventricular tachycardia	2 (3.0%)	0	2 (1.5%)
Atrial flutter	0	1 (1.4%)	1 (0.7%)
Pulseless electrical activity	1 (1.5%)	0	1 (0.7%)
Sinus bradycardia	1 (1.5%)	0	1 (0.7%)
Supraventricular tachycardia	0	1 (1.4%)	1 (0.7%)
Cardiac murmur	1 (1.5%)	0	1 (0.7%)
ECG signs of myocardial ischaemia	0	1 (1.4%)	1 (0.7%)
Electrocardiogram QT prolonged	1 (1.5%)	0	1 (0.7%)
Radial pulse abnormal	0	1 (1.4%)	1 (0.7%)

Data is presented as n (%) where n is the number of subjects, % is the percentage of subjects within a treatment group.

eTable 4. Summary of New York Heart Association Classification

Visit Classification	NP202 (N=66) n (%)	Placebo (N=71) n (%)	Overall (N=137) n (%)
Visit 2 (Day 14)			
Number assessed	56	66	122
I	42 (75.0%)	43 (65.2%)	85 (69.7%)
II	12 (21.4%)	22 (33.3%)	34 (27.9%)
III	2 (3.6%)	1 (1.5%)	3 (2.5%)
IV	0	0	0
Visit 5 (Day 90)			
Number assessed	51	62	113
I	40 (78.4%)	56 (90.3%)	96 (85.0%)
II	11 (21.6%)	6 (9.7%)	17 (15.0%)
III	0	0	0
IV	0	0	0
Early Withdrawal			
Number assessed	3	4	7
I	2 (66.7%)	4 (100%)	6 (85.7%)
II	0	0	0
III	1 (33.3%)	0	1 (14.3%)
IV	0	0	0
End of Study (Day 120)			
Number assessed	51	62	113
I	42 (82.4%)	57 (91.9%)	99 (87.6%)
II	9 (17.6%)	5 (8.1%)	14 (12.4%)
III	0	0	0
IV	0	0	0

Data is presented as n (%) where n is the number of subjects, % is the percentage of subjects within a treatment group.

eTable 5. Change in Cardiac Biomarker NT-proBNP

	NT-proBNP (ng/L)	**NP202**	**Placebo**	**Treatment difference p-value**
Baseline	Mean (SD)	1933.92 (1891.853)	2470.65 (2398.146)	0.1629
Day14	Mean (SD)	1727.39 (1282.019)	1848.50 (1378.635)	0.6293
	Change from Baseline (SD)	-193.48 (1484.119)	-344.51 (1164.685)	0.5599
Day 30	Mean (SD)	1314.91 (1084.954)	1265.46 (924.478)	0.7915
	Change from Baseline (SD)	-579.06 (1348.244)	-904.86 (1437.477)	0.2256
Day 60	Mean (SD)	799.85 (854.790)	683.80 (477.762)	0.3728
	Change from Baseline (SD)	-873.77 (1122.854)	-1534.07 (1764.695)	*0.0298*
Day 90	Mean (SD)	633.80 (914.544)	570.18 (487.813)	0.6434
	Change from Baseline (SD)	-1037.63 (898.240)	-1721.75 (1770.300)	*0.0169*
Day 120	Mean (SD)	581.98 (922.018)	468.16 (348.217)	0.3862
	Change from Baseline (SD)	-1047.61 (935.348)	-1855.59 (1848.304)	*0.0073*

Abbreviations: NT-proBNP=brain natriuretic peptide type B; SD=standard

eTable 6. Change in Cardiac Biomarker Troponin T

	Troponin T (ng/L)	**NP202**	**Placebo**	**Treatment difference p-value**
Baseline	Mean (SD)	3000.20 (1819.500)	3458.59 (2108.394)	0.1949
	Mean (SD)	93.24 (132.508)	92.52 (121.521)	0.9758
Day14	Change from Baseline (SD)	-2729.41 (1797.626)	-3320.06 (1814.337)	0.0953
Day 30	Mean (SD)	31.04 (53.012)	35.92 (45.920)	0.5960
	Change from Baseline (SD)	-2719.21 (1784.823)	-3280.55 (1876.283)	0.1144
Day 60	Mean (SD)	19.57 (12.119)	22.61 (15.767)	0.2771
	Change from Baseline (SD)	-2669.64 (1845.985)	-3319.06 (1904.530)	0.0874
Day 90	Mean (SD)	15.37 (8.962)	18.90 (12.936)	0.1082
	Change from Baseline (SD)	-2607.76 (1531.102)	-3395.65 (1891.258)	*0.0240*
Day 120	Mean (SD)	15.69 (12.178)	18.42 (14.080)	0.2927
	Change from Baseline (SD)	-2531.51 (1386.457)	-3501.66 (1848.879)	*0.0040*

eTable 7. Investigators and Affiliated Institutions

Name of Site and Investigator	Address of Site
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Liverpool Hospital Prof John French	Elizabeth St Liverpool NSW 2170 Australia
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