ENTIRE TRIAL SPONSORED BY EU-FP7 GRANT

MITOCARE STUDY

Multicenter, randomized, double-blind, placebo controlled study to assess safety and efficacy of TRO40303 for reduction of reperfusion injury in STEMI patients undergoing primary PCI

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MitoCare – EU FP7 HEALTH-F2-2010-261034

DECLARATION OF INTEREST

- EU-FP7 grant "MITOCARE" (2010-2013)

MITOCARE

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Multicenter, randomized, double-blind, placebo controlled study to assess safety and efficacy of TRO40303 for reduction of reperfusion injury in STEMI patients undergoing primary PCI

Rationale: TRO40303 has been shown to reduce infarct size by 50% in rat and mouse models, and to improve LVEF at 24h and 1 month in these models. It has also shown protective effects on isolated *human* cells.

Mechanism: The mitochondrial permeability transition pore is believed to be a promising target for preventing reperfusion injury.TRO40303 has shown to inhibit the opening of this transition pore.

Scope and Enrolment Period of the Study:
October 2011-September 2013
10 interventional sites in Denmark, France, Norway, Sweden.

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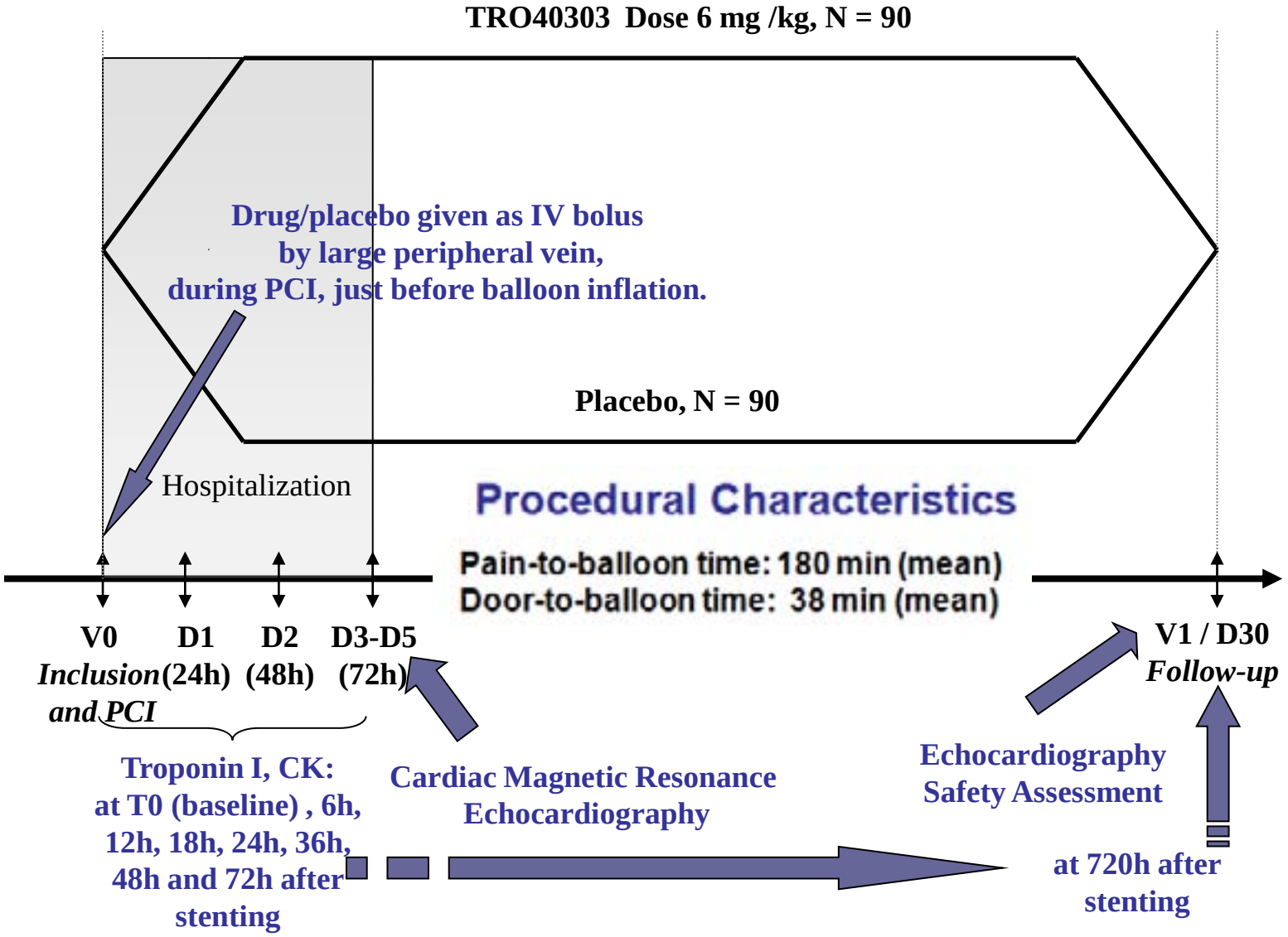
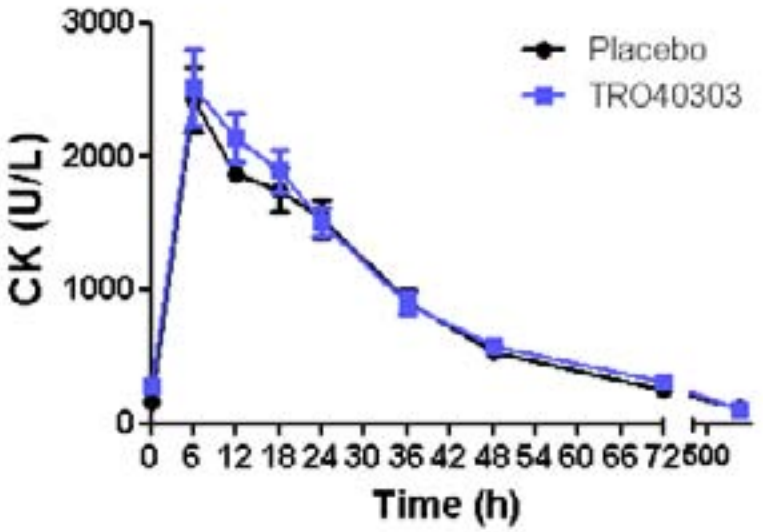
Study Design

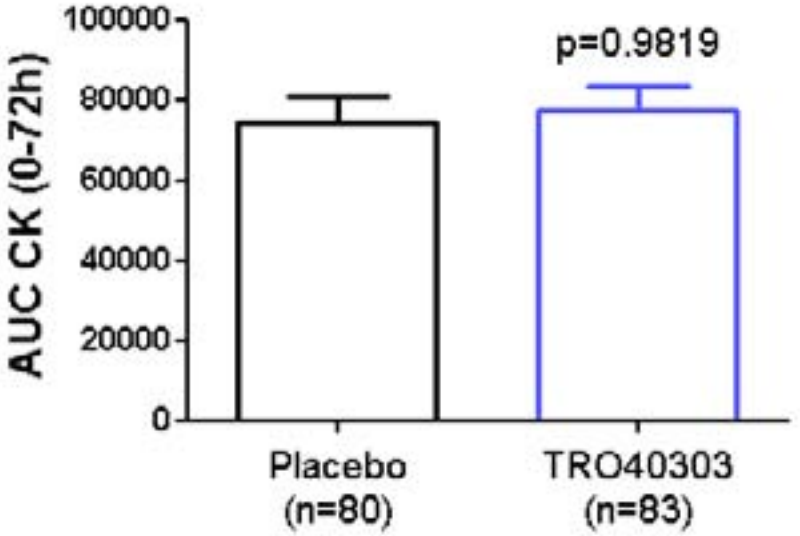
INCLUSION CRITERIA:

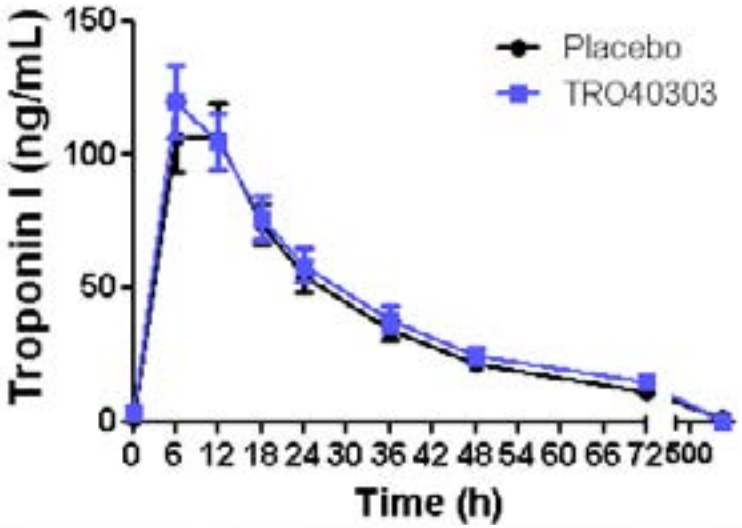
First time STEMI, presenting within 6h of onset of pain
Clinical decision to treat with primary PCI
Occlusion / TIMI flow 0-1 in culprit artery before PCI

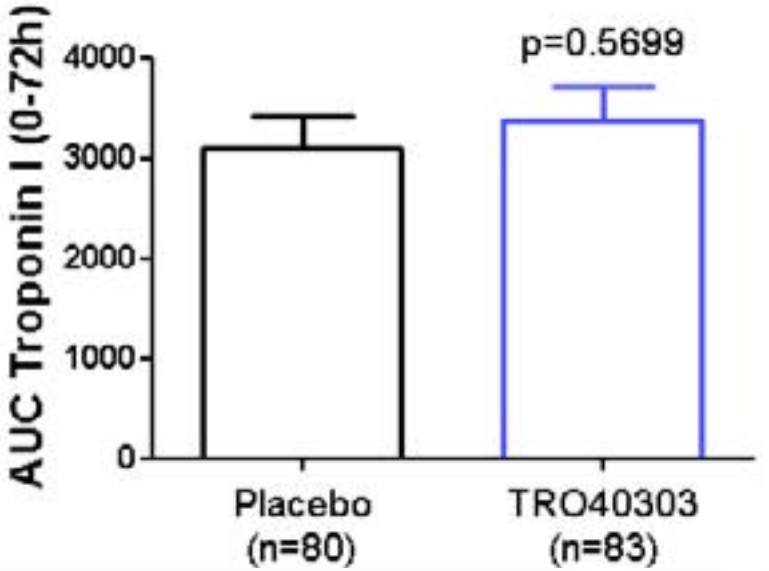


Study Results: Co-primary Endpoint









MRI Endpoints

	Placebo	TRO40303	N/gp	P (*)
Main MRI endpoint: Myocardial salvage index (MSI)	0.58 (0.2-0.9)	0.52 (0.2-0.8)	43/50	0.1000
Infarct Size/Left Ventricle	0.15 (0.0-0.4)	0.17 (0.1-0.4)	43/50	0.1034
Infarct Size (gr)	20.01 (1.8-82.9)	21.88 (3.1-62.1)	43/50	0.1650
Microvascular Obstruction	0.02 (0.0-0.1)	0.02 (0.0-0.2)	43/50	0.8512
LV End Diastolic Volume (ml)	178.22 (73.7-274.6)	177.02 (73.7-288.7)	54/57	0.9966
LV End Systolic Volume (ml)	93.1 (37.4-186.8)	96.25 (31.9-185.1)	54/57	0.6485
LV Ejection Fraction	0.48 (0.2-0.6)	0.46 (0.3-0.6)	54/57	0.1526

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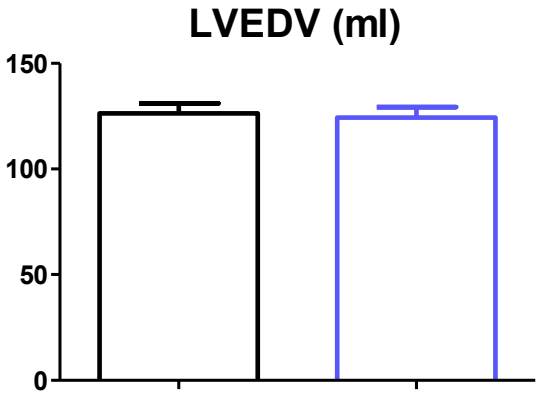
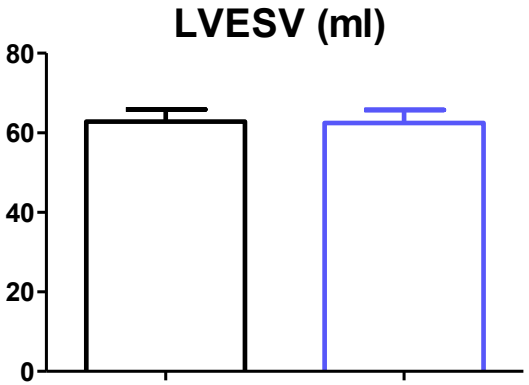
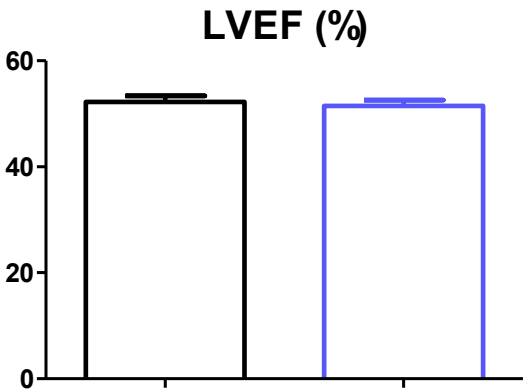
Additional Secondary Endpoint: Echocardiography at D30







Placebo

TRO40303

ANCOVA (Time to PCI and culprit artery in the model, center as random effect)	P value
LV end Diastolic Volume (ml)	0.8789
LV end Systolic Volume (ml)	0.8048
LV end Ejection Fraction (%)	0.2784

- Data presented as mean +/- SEM
- Number patients analysed = 105 for LVEDV; 104 for LVESD; 139 for LVEF

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MITOCARE - Conclusions

- The MITOCARE trial did not show any protective effect of TRO40303 compared to placebo in preventing reperfusion injury in STEMI patients treated with primary PCI
- A high standard of care accounted for the relatively small infarct size after primary PCI, leaving little room for improvement
- These results combined with the many failures in the field raise a provocative issue: whether reperfusion injury occurs at all in man, and, if it does, whether this type of injury really accounts for a significant part of the remaining infarct

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