



Aker University Hospital
Oslo, Norway



F.I.R.E. study

A Multicenter, Double-blind, Randomized, Placebo-Controlled Study to Measure the Effect of FX06 (a fibrin-derived peptide B β 15-42) on Ischemia-REperfusion Injury in Patients Undergoing Primary Percutaneous Coronary Intervention

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F.I.R.E. – a Phase II trial of FX06 in STEMI

Background

- Treatment of choice for STEMI = early reperfusion by PCI or thrombolysis
- PCI can lead to reperfusion injury
- No successful pharmacologic strategies to mitigate reperfusion injury

FX06: A Novel Compound

- Small peptide derived from the human fibrin sequence
- Prepared by solid phase peptide synthesis

FX06 has anti-inflammatory and vasculoprotective function

F.I.R.E. - Rationale

- To investigate the cardioprotective efficacy of FX06 as an adjunct to reperfusion therapy in patients with acute STEMI
- To assess safety and tolerability

F.I.R.E. across Europe



Design

- Exploratory „Proof-of-Concept“, Double-blind, placebo-controlled multicenter study

Dose: 400 mg FX06 i.v. vs. Placebo

Patients : 234 STEMI – randomized

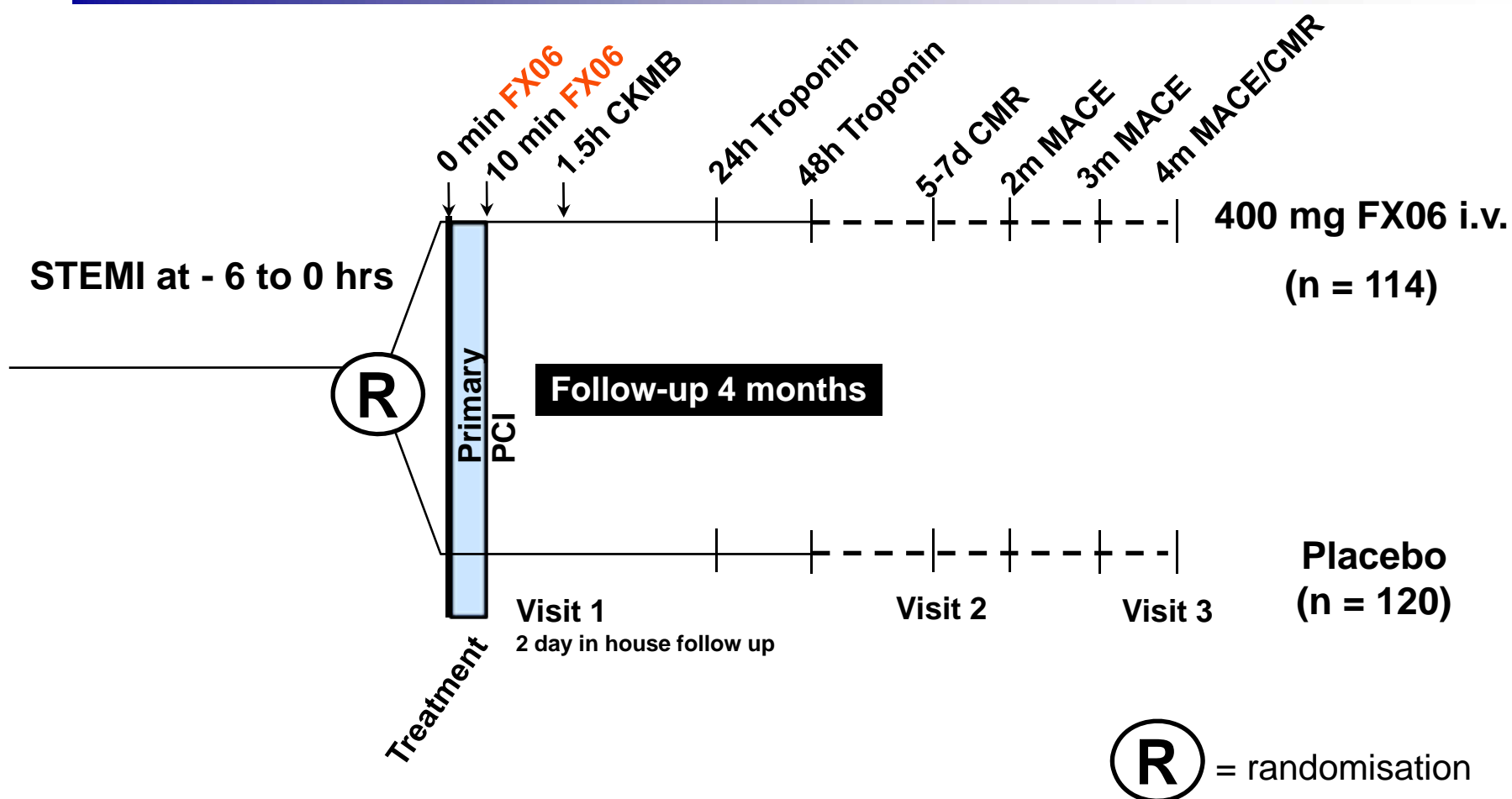
Inclusion Criteria

- First MI
- Primary PCI indicated per standard
- Single index lesion with complete occlusion (TIMI flow 0/I) of one target vessel
- Onset of symptoms to balloon time < 6 hrs
- ST elevation of at least 2 mm in at least 3 leads on 12-lead ECG

Exclusion Criteria

- Chest pain or angina in last 24 hours
- Administration of thrombolytic agent
- Cardiogenic shock
- Contraindication to CMR
- Known renal dysfunction
- Previous CABG
- History of CHF
- BMI > 35

Study flowchart



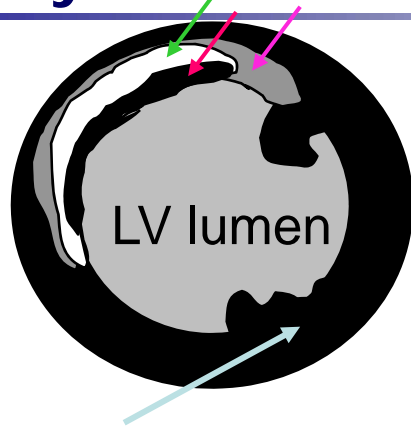
PRIMARY OUTCOME MEASURE:

- Infarct size measured by CMR at 5 days

SECONDARY OUTCOME MEASURE

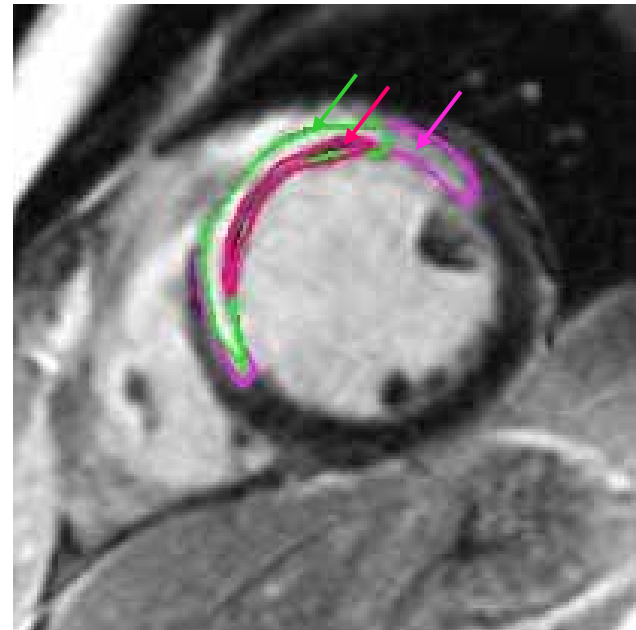
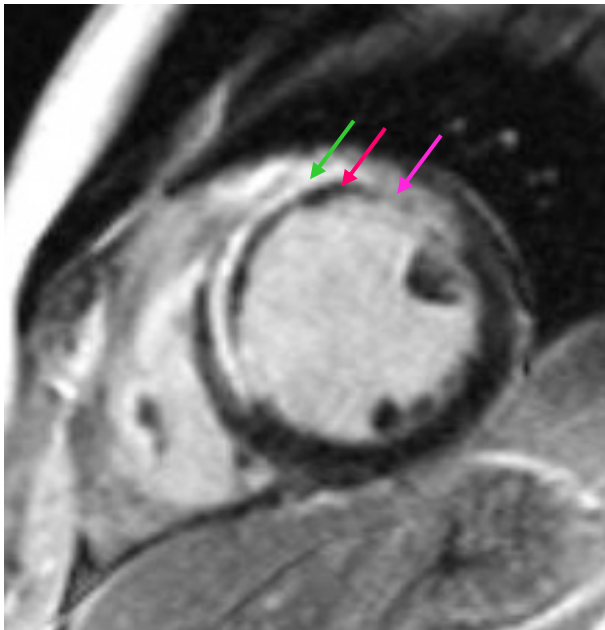
- infarct size at 4 mth's, biomarkers, MACE

Acute Myocardial Infarction Imaged with LGE CMR



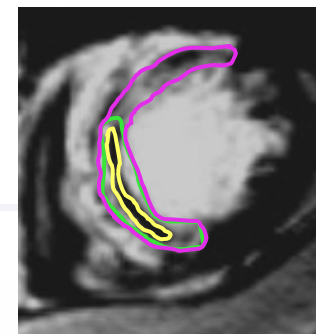
normal myocardium

- ↙ MVO zone
- ↘ necrotic core zone
- ↙ total LGE zone

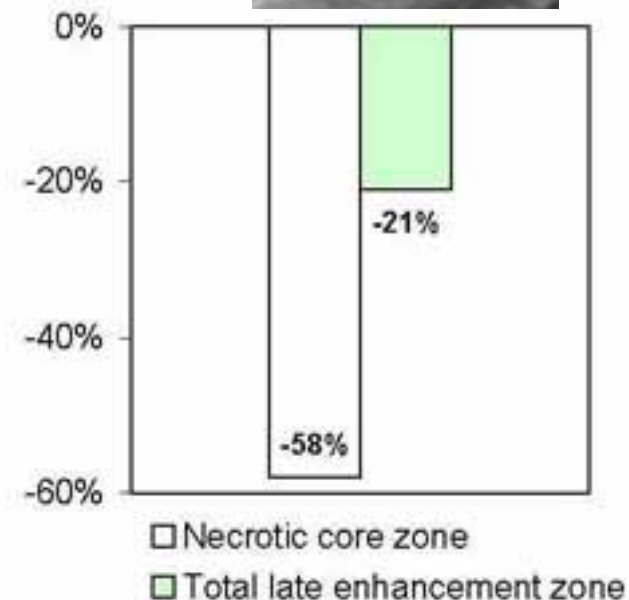
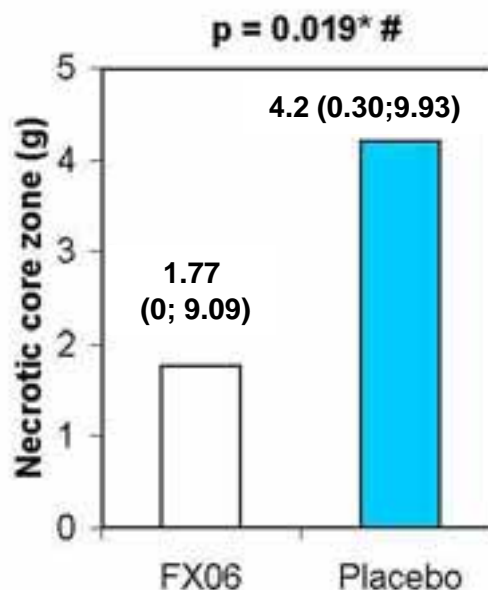
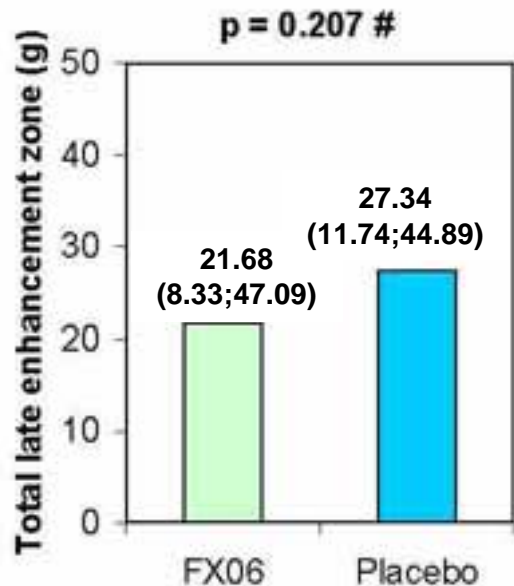


5 days post PCI: No difference in total late enhancement zone

Necrotic core significantly reduced (ITT Population)



Median with 25- and 75-percentile

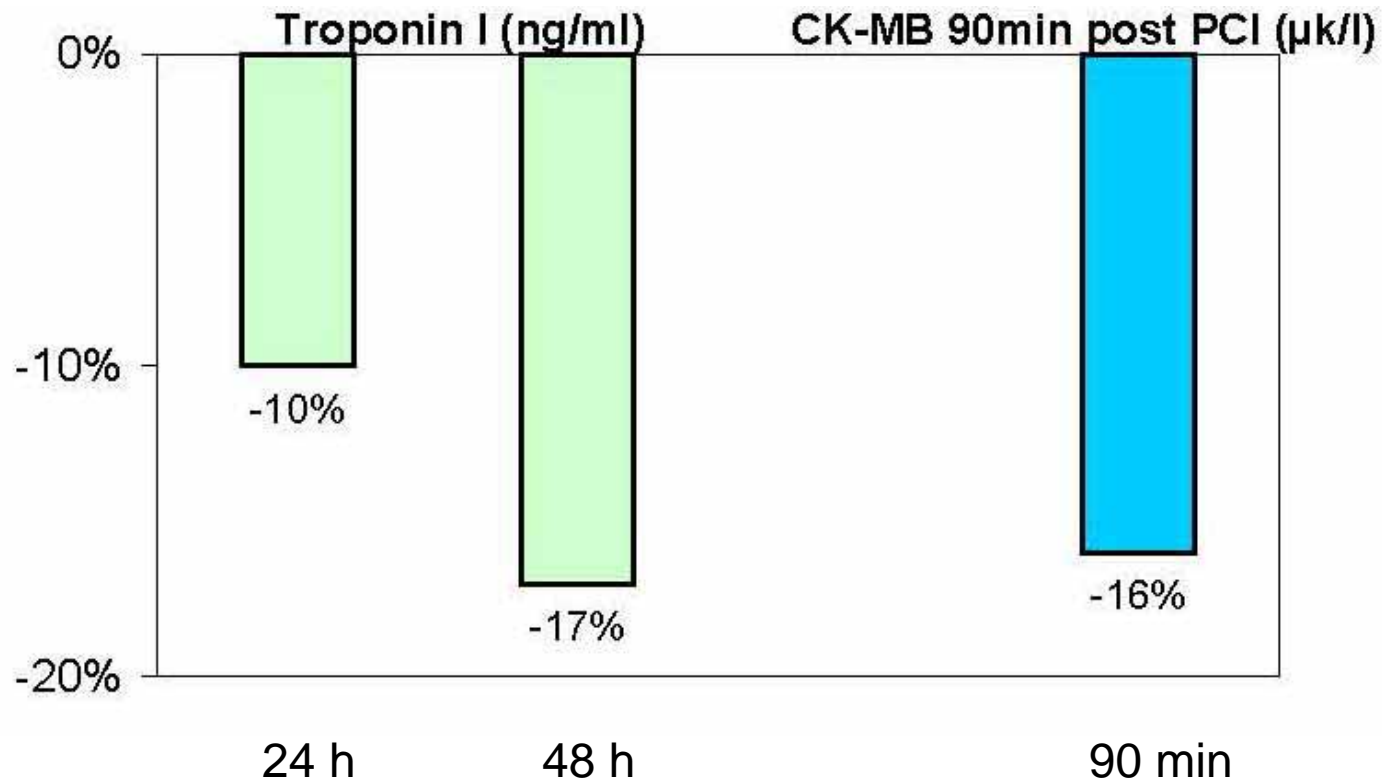


* statistically significant
Wilcoxon rank sum test

LV ejection fraction at V2 and V3	FX06	Placebo
LVEF at 5 days:	46.7 %	46.6 %
LVEF at 4 months:	49.1%	48.9 %

LVEF 4 months post-PCI well preserved in all pats: successful recanalisation.

No significant reduction in biochemical markers of cardiac necrosis



Clinical outcomes and safety

Positive signals in clinical outcome parameters	FX06 N	Placebo N
Cardiac death	2	5
Serious adverse cardiac related events - day 30	15	25
Serious adverse cardiac related events - overall	21	29
Composite of cardiac death and new onset heart failure/pulmonary edema	5	10

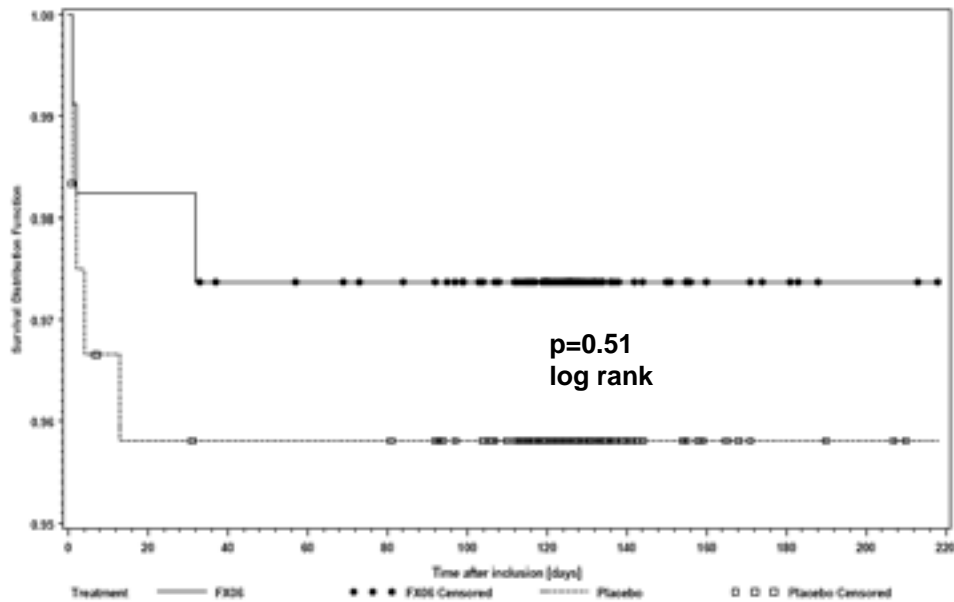
Safety	FX06 (N=114)		Placebo (N=120)	
	N	%	N	%
All cause mortality	3	2.6%	5	4.2%

No difference in SAEs and AEs compared to placebo

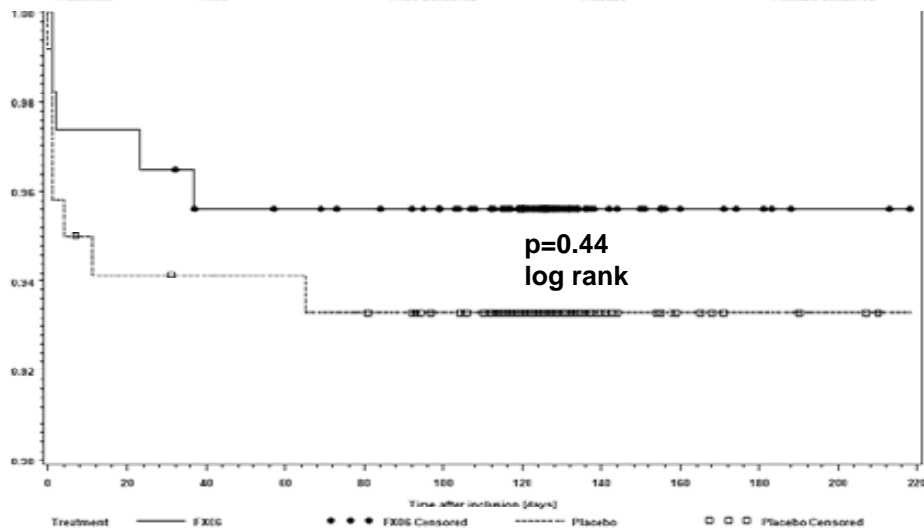
No safety signals on:

- arrhythmogenic potential
- thrombogenic potential
- hypotension

Kaplan Meier plots



Overall survival



Time to cardiac death or onset of heart failure

Conclusion:

FX06 results in the following effects vs. placebo.....

Imaging endpoints and biomarkers:

- **Primary endpoint: Change in LGE zone not statistically significant**
- **Necrotic core infarct zone at 5 days significantly reduced (-58%, $p < 0.025$)**
- **Incidence of microvascular obstruction (27.6% versus 37.5%) not significantly different**
- **Scar mass 4 mths post PCI not significantly different**
- **LV-EF not significantly changed at 4 mths**
- **No significant change in CK-MB at 90 min (-16%) and Troponin I at 24 (-10%) and 48 hrs (-17%) post PCI**

Clinical endpoints:

- **Incidence of cardiac death: 2 vs. 5**
- **Major cardiovascular adverse events: 21 vs. 29**
- **Combined incidence of cardiac death and new onset CHF: 5 vs. 10**

- **This study may suggest a cardioprotective role of FX06 as an adjunct treatment to PCI**
- **Effect of FX06 on necrotic infarct zone most likely achieved by amelioration of reperfusion injury**
- **These findings from explorative study may encourage scrutinization in a larger trial**

The FIRE team

- **FIRE Steering Committee:**

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- **CMR CORE LABORATORY**

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- **ECG CORE LABORATORY**

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- **Data Safety Monitoring Board (DSMB):**

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Conflicts-of-Interest: DA received honoraria from Fibrex Medical