

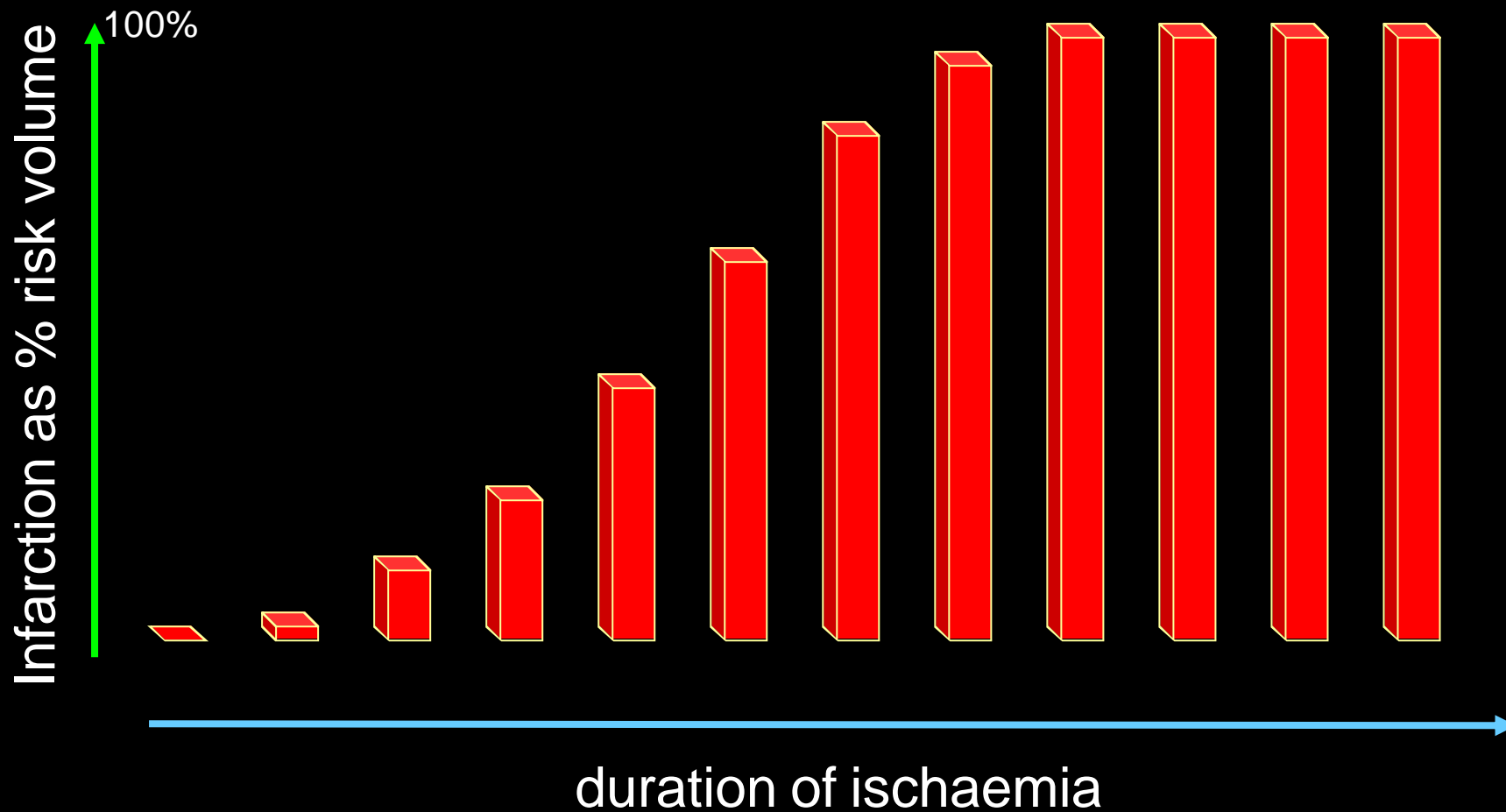
## F.I.R.E. study

A Multicenter, Double-blind, Randomized, Placebo-Controlled Study to Measure the Effect of **EX06** (a fibrin-derived peptide BB15-42) on **I**schemia-**RE**perfusion Injury in Patients Undergoing Primary Percutaneous Coronary Intervention

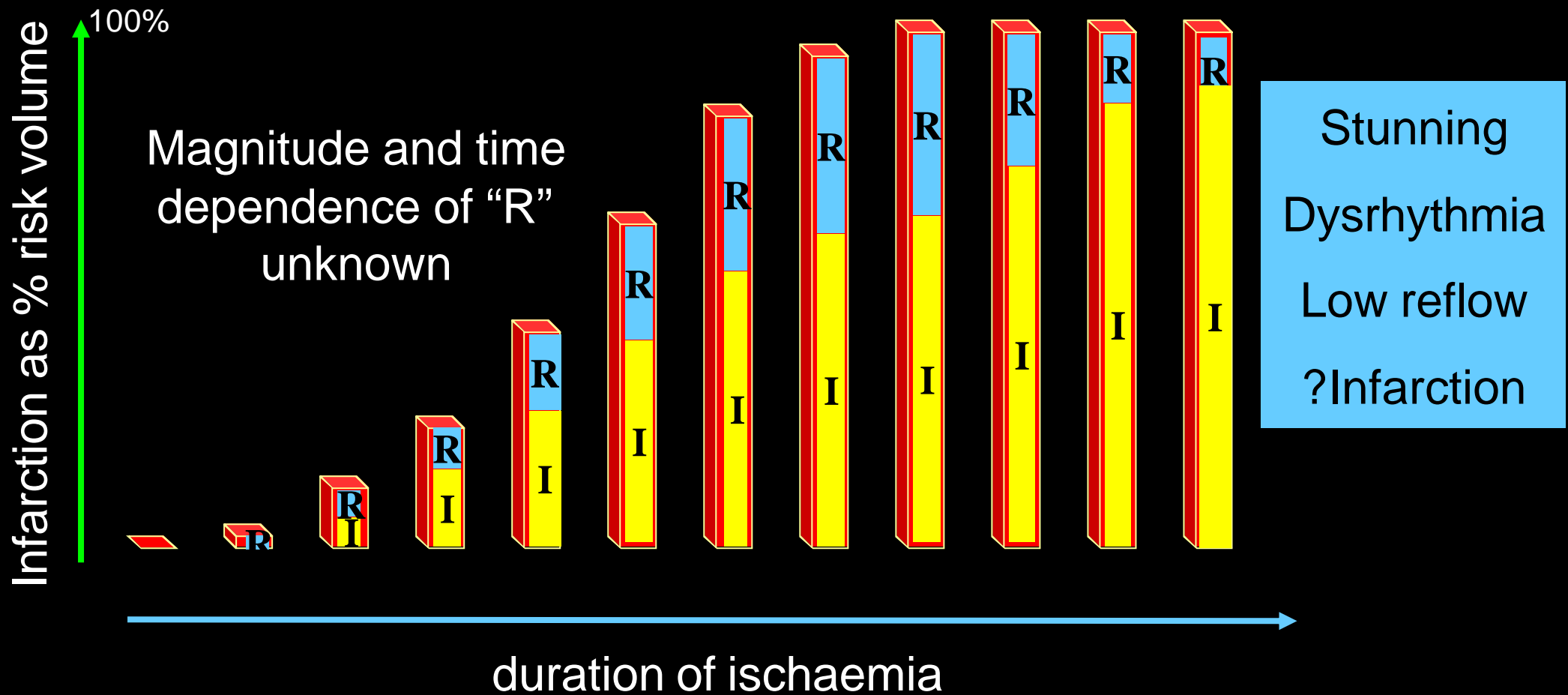
**Discussant Michael Marber**  
**King's College London**

No Conflicts to Declare

# Concept of Separate Ischaemia (I) and Reperfusion (R) Injury



# Concept of Separate Ischaemia (I) and Reperfusion (R) Injury



# Anti-inflammatory Interventions at Reperfusion in STEMI

Intervention	No of pts	Symptom duration (hr)	Reperfusion	Result
Anti-CD18 Ab (LIMIT-AMI)	394	3.5	Lysis	<u>No effect</u> on MI size, coronary blood flow or ST resolution
Anti-CD11 and 18 Ab (HALT-MI)	420	3.8	PCI	<u>No effect</u> on MI size, TIMI grade, or events
Anti-P-selectin Ab (RAPSODY)	598	<6	Lysis	<u>No effect</u> on MI size, LVEF or events. ST resolution slowed
Anti-cell adhere RheothRx (CORE)	2,948	3.5	Lysis	<u>No effect</u> on MI or shock. Worse LV and renal function
Anti-C5 Ab (COMPLY)	943	2.7	Lysis	<u>No effect</u> on CK-derived MI size or MACE
Anti-C5 Ab (COMMA)	960	3.2	PCI	<u>No effect</u> on CK-derived MI size or MACE
Anti-C5 Ab (APEX-AMI)	5,745	3.2	PCI	<u>No effect</u> on mortality or MACE

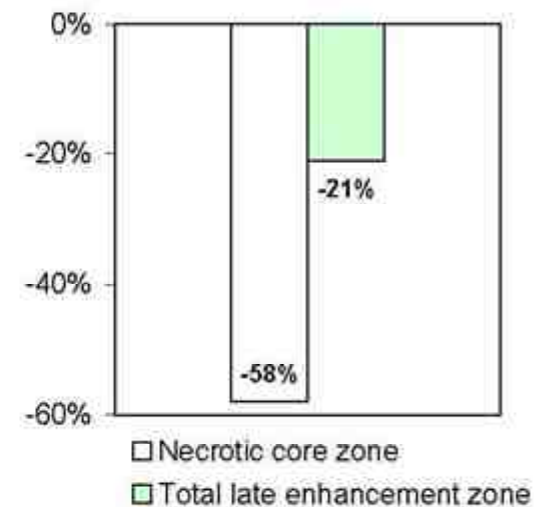
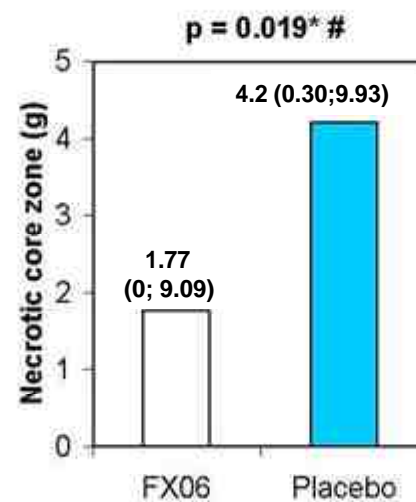
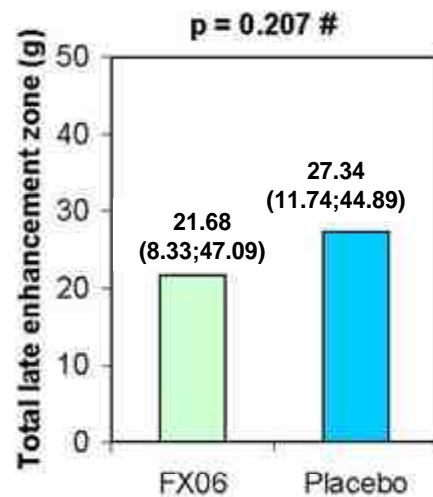
Adapted from Dirksen et al Cardiovasc Res 2007;74:343-55 and Yellon & Hausenloy NEJM 2007;357:1121-35

# Main Positive Finding of FIRE

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

Necrotic core significantly reduced (ITT Population)

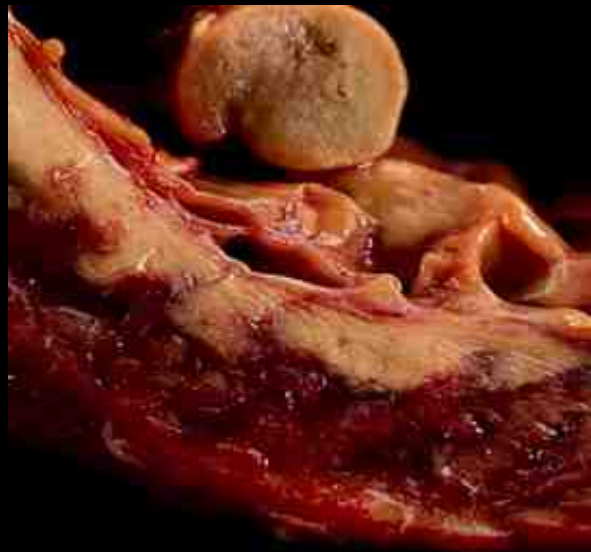
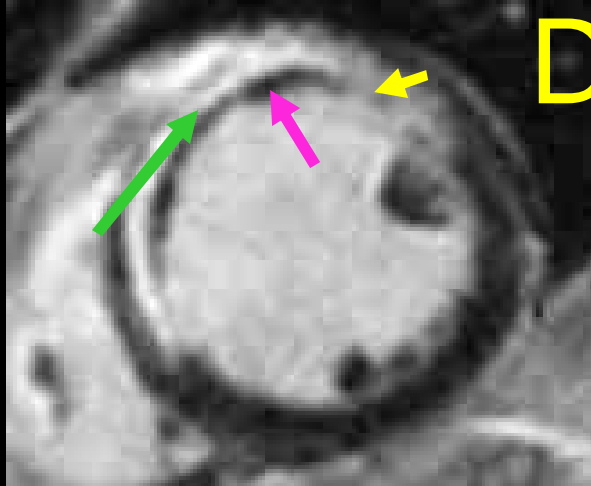
Median with 25- and 75-percentile



\* statistically significant  
# Wilcoxon rank sum test

- Incidence of microvascular obstruction (MVO): 27.6% versus 37.5% (not statistically significant)

# Use of Necrotic Core Zone at Day 5 as Endpoint



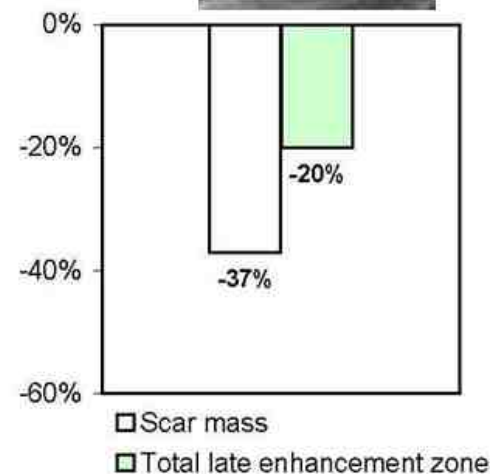
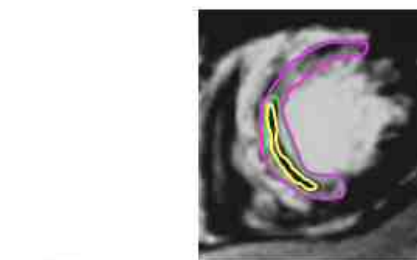
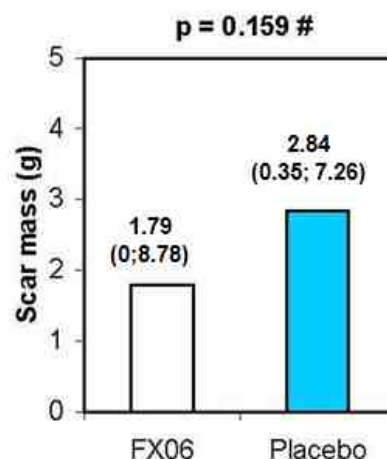
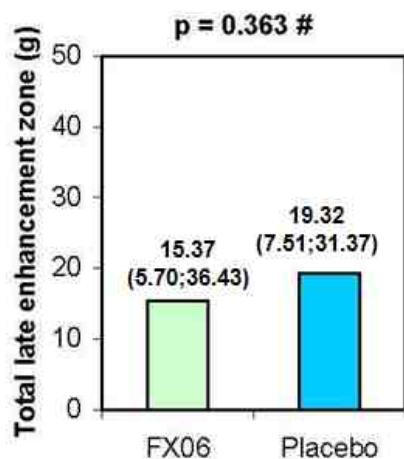
- Principal Endpoint is total LGE (ns)
- Necrotic core only 10% total LGE
- Sub- or ob-jective threshold?
- Usually expressed as % LV mass
- MVO part of necrotic core & NS
- Prespecified analysis
- Biological meaning
- Oedema + necrosis
- Corroborative late signal ?

# No Lasting Effect of Early Difference

**4 mths post PCI: No difference in**

- **Total late enhancement zone**
- **Scar mass** (ITT population)

**Median with 25- and 75-percentile**



# 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.**

# Conclusions

- Another negative study of an anti-inflammatory intervention during reperfusion
  - Short pain to balloon time, high use of 2<sup>nd</sup> ary prev meds, v.well preserved LV function, low mortality
- FX06 appears safe
- Trends in Tn/CK/MRI require verification

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Anti-VE Cadherin Fibrin fragment (FIRE)	234	Approx 3	PCI	<u>No effect</u> on MI size, LVEF, or MACE