Abstract 13 Figure 1

Abstract 13 Figure 2

14 DYNAMIC CHANGES OF OEDEMA AND LATE GADOLINIUM ENHANCEMENT AFTER ACUTE MYOCARDIAL INFARCTION AND THEIR RELATIONSHIP TO FUNCTIONAL RECOVERY AND SALVAGE INDEX

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Introduction Changes in myocardial tissue in acute ischaemia are dynamic and complex and the characteristics of myocardial tissue on cardiovascular magnetic resonance (CMR) in the acute setting are not fully defined. We investigated changes in oedema and late gadolinium enhancement (LGE) with serial imaging early after acute

Abstract 14 Figure 1

MI, relating these to global and segmental myocardial function at 6 months.

Methods and Results CMR scans were performed on 30 patients with ST elevation MI (STEMI) treated by primary PCI at each of 4 time points: 12–48 h (TP1); 5–7 days (TP2); 14–17 days (TP3); and 6 months (TP4). All patients showed oedema at TP1. The mean volume of oedema (% LV) was 37 ± 16 at TP1 and 39 ± 17 at TP2

Abstract 14 Figure 2

with a reduction to 24 ± 13 ($p < 0.01$) by TP 3. Myocardial segments with oedema also had increased signal on LGE at TP1 ($\kappa = 0.77$; $p < 0.001$). At TP1, the proportion of segments with wall motion impairment increased in relation to the extent of both myocardial oedema ($p < 0.01$) and LGE ($p < 0.01$). The volume of LGE decreased significantly between TP1 and TP4 ($27 \pm 15\%$ vs $22 \pm 12\%$; $p = 0.002$). Of segments showing LGE at 48 h, 50% showed resolution by 6 months. In segments with such a reduction in LGE, 65% also showed improved wall motion ($p < 0.0001$). The area of LGE measured at 6 months correlated more strongly with 48-h troponin ($R^2 = 0.84$; $p < 0.01$) than at TP1 ($R^2 = 0.5$). The difference in LGE between TP1 and TP4 had profound effects on the calculation of salvage index ($26 \pm 21\%$ at TP1 vs $42 \pm 23\%$ at TP4; $p < 0.02$).

Conclusions (1) Myocardial oedema was unchanged over the first week but decreased by 15 days; (2) a large majority of segments that were positive for oedema also showed LGE, assessed at 12–48 h; (3) In 46% of patients, LGE present on early scans had diminished in size by 6 months, (4) resolution of LGE was associated with improvement in function; (5) the reduction in LGE at the later time had a profound effect on the calculation of salvage index, which varied by up to $\sim 60\%$, depending on the time point used. (6) From a clinical perspective, the use of acute LGE may severely underestimate salvaged myocardium and should not be used to predict recovery of myocardial function.

15 INVESTIGATION OF IL-1 INHIBITION IN PATIENTS PRESENTING WITH NON-ST ELEVATION MYOCARDIAL INFARCTION ACUTE CORONARY SYNDROMES (THE MRC ILA HEART STUDY)

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Background Inflammatory mechanisms are involved in both coronary atherogenesis and its presentation as acute coronary syndromes (ACS). To date, drugs used at the time of ACS, or for primary and secondary prevention have not primarily targeted inflammatory mechanisms. Studies with aspirin and statin drugs indicate that anti-inflammatory properties of these compounds may contribute to their beneficial effects. Pre-clinical studies from our group have indicated that the pro-inflammatory cytokine IL-1 drives a number of vascular events relevant to coronary artery disease and ACS. IL-1 can be inhibited by IL-1 receptor antagonist (IL-1ra, Anakinra, Amgen) which is licensed for the treatment of rheumatoid arthritis.

Aims To investigate the effects of interleukin-1 receptor antagonist (IL-1ra) on inflammatory biomarkers in patients with ACS <48 h from symptom onset, and to evaluate the safety and tolerability of treatment.

Design and methods The UK MRC ILA-HEART study is an investigator-initiated, non-industry sponsored, phase 2, multi-centre, placebo-controlled trial, comparing the IL-1ra (100 mg) with matching placebo given as a single, daily subcutaneous injection over 2 weeks. The primary outcome of the study was area under the curve (AUC) of high sensitivity CRP (hs-CRP) over the first 7 days of treatment, and the main secondary outcomes are AUC of troponin and safety and compliance of trial treatment. Patients were encouraged to self-administer trial treatment, and underwent daily assessment of hs-CRP, troponin, von Willebrand factor and other biomarkers up to 7 days, and again at 2 weeks and 30 days. Patients were followed up to 12 months for safety (Abstract 15 table 1).

Abstract 15 Table 1 Log transformed values for the primary and secondary outcomes

Variable	Active n	Active mean (SD)	Placebo n	Placebo mean (SD)	p
hsCRP AUC (days 1–7)	82	3.51 (1.42)	78	3.55 (1.46)	0.86
hsCRP at day 7	78	1.03 (1.46)	78	1.09 (1.91)	0.83
hsCRP at day 14	77	1.14 (1.54)	76	0.89 (1.56)	0.32
hsCRP at day 30	76	1.13 (0.32)	76	0.92 (1.15)	0.30
Troponin AUC (days 1–7)	82	1.35 (1.88)	78	1.50 (1.96)	0.61
Troponin at day 14	77	−3.73 (2.31)	76	−4.14 (2.35)	0.27
Troponin at day 30	76	−4.83 (2.44)	76	−4.74 (2.51)	0.82
vWF AUC (days 1–3)	89	1.33 (0.35)	84	1.31 (0.35)	0.66
vWF at day 14	77	0.36 (0.35)	84	0.28 (0.41)	0.23
vWF at day 30	78	0.37 (0.34)	75	0.29 (0.43)	0.19
IL-6 AUC (days 1–3)	86	2.62 (1.13)	83	2.56 (1.02)	0.74
IL-6 at day 14	77	1.32 (1.35)	77	0.92 (0.75)	0.028
IL-6 at day 30	73	1.22 (0.92)	75	1.08 (0.77)	0.31

Results Five UK centres randomised 182 patients with non-ST elevation (NSTEMI) ACS to IL-1ra or placebo. Enrolment completed in March 2010. Mean age was 61 years, 32% female, 28% prior MI, 15% diabetes, 90% were receiving a statin at the time of randomisation and 64% had early PCI or CABG. Compliance was good with 85% of patients receiving daily injections during the first 7 days, and 70% of patients were able to self-administer the injections. Injection site reactions reported as adverse events occurred in 14% of patients. There was no significant difference in area under the curve for hsCRP between active and placebo groups. The MACE and serious adverse event rates are shown in Abstract 15 table 2.

Abstract 15 Table 2 MACE and other SAE

Event	Active (n (95% CI))	Placebo (n (95% CI))	p
MACE at 30 days	6 (0.19 to 1.79)	10 (1)	0.35
MACE at 3 months	10 (0.32 to 1.84)	13 (1)	0.54
MACE at 1 year	20 (0.59 to 2.22)	18 (1)	0.69
MI (%)	3.26	7.78	0.18
Stroke (%)	1.09	0	1.00
Death (%)	4.35	4.44	1.00
CV hospitalisation (%)	19.86	25	0.31
Revascularisation (%)	69.56	60	0.8
Injection site reactions (%)	15.22	15.56	0.95
Other SAE (%)	47.83	44.44	0.65

Discussion NSTEMI ACS treated with all the current evidenced-based therapies still has significant recurrent events. MRC ILA-HEART is the first study to evaluate the effects of the anti-inflammatory IL-1ra in ACS. The data indicates that despite encouraging pre-clinical evidence, the inflammatory driver for NSTEMI-ACS is not IL-1 mediated.

16 ACUTE STENT THROMBOSIS RESULTING IN ST ELEVATION MYOCARDIAL INFARCTION (STEMI) IS ASSOCIATED WITH WORSE CLINICAL OUTCOMES THAN STEMI DUE TO NATIVE CORONARY THROMBOSIS

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Background Stent thrombosis (ST) is a recognised cause of ST Elevation Myocardial infarction (STEMI) in patients with previous