

Dinesh Kadariya¹, George F Wohlford^{1,2}, Ai-Chen Ho², Alessandra Vecchié¹, Cory R Trankle¹, Leo F Buckley³, Justin Canada¹, Salvatore Carbone^{1,4}, Roshanak Markley¹, Jeremy Turlington¹, Nayef Abouzaki¹, Darryn Appleton⁵, Michael J. Lipinski⁶, Benjamin W Van Tassel², Antonio Abbate¹

¹Virginia Commonwealth University, Pauley Heart Center, Division of Cardiology, Department of Internal Medicine, Richmond, VA, USA. ²Department of Pharmacotherapy and Outcome Sciences, School of Pharmacy, Virginia Commonwealth University, Richmond, VA, USA. ³Division of Cardiovascular Medicine and Department of Pharmacy Services, Brigham and Women's Hospital, Boston, MA, USA. ⁴Department of Kinesiology & Health Sciences, College of Humanities & Sciences, Virginia Commonwealth University, Richmond, Virginia, USA. ⁵Virginia Cardiovascular Specialists, Richmond, USA. ⁶Medstar Research Institute, Washington, Dc, USA

Background

- STEMI is associated with an intense acute inflammatory response that may have deleterious effects on the heart that opposes the advantageous effects of tissue repair.
- An association with an increased risk of death and heart failure (HF) remains despite many advances in care for these patients.
- It remains to be determined if a selective and timely blunting of the inflammatory response can improve hard patient outcomes beyond prognostic inflammatory biomarkers

Methods

- We analyzed the effect of recombinant interleukin-1 receptor antagonist (Anakinra) 100 mg once or twice daily administered early after reperfusion in a patient level pooled analysis of 3 clinical trials
- Treatment with anakinra was continued for 14 days
- Enrollment criteria and study procedures did not significantly differ across the three studies.

KEY EXCLUSION CRITERIA

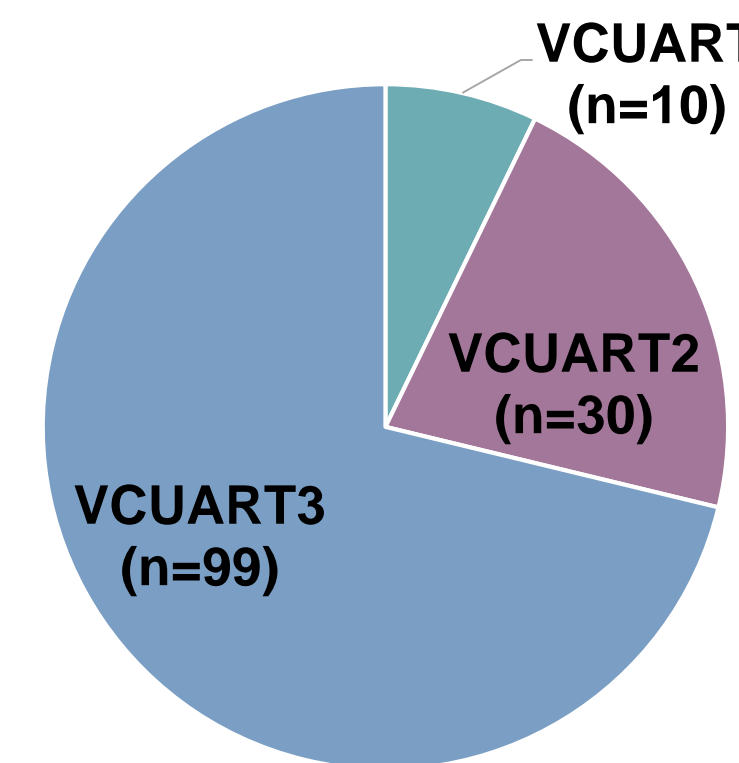
- Cardiac arrest
- Unsuccessful PCI
- Hemodynamic instability
- Previous Q-wave infarction
- Pre-existing severe congestive heart and/or severe left ventricular (LV) dysfunction (LVEF <20%)
- Severe aortic or mitral valve disease
- Pregnancy
- Chronic infections
- Autoinflammatory or autoimmune disease

KEY INCLUSION CRITERIA

- Age ≥18 years old
- Acute (<24 hours) onset of chest pain
- Electrocardiographic evidence of ST-segment elevation myocardial infarction
- Planned or completed angiography for urgent percutaneous coronary intervention

- High-sensitivity C-reactive protein (CRP) were obtained at baseline, 72 hours and 14 days
- Area under the curve (AUC₀₋₁₄) was estimated using these 3 data points
- Clinical events were adjudicated by an independent committee blinded to treatment allocation
- Data for anakinra once daily and anakinra twice daily were pooled into a single anakinra group
- Kaplan-Meier survival analyses were conducted and intervention groups compared using a log rank test

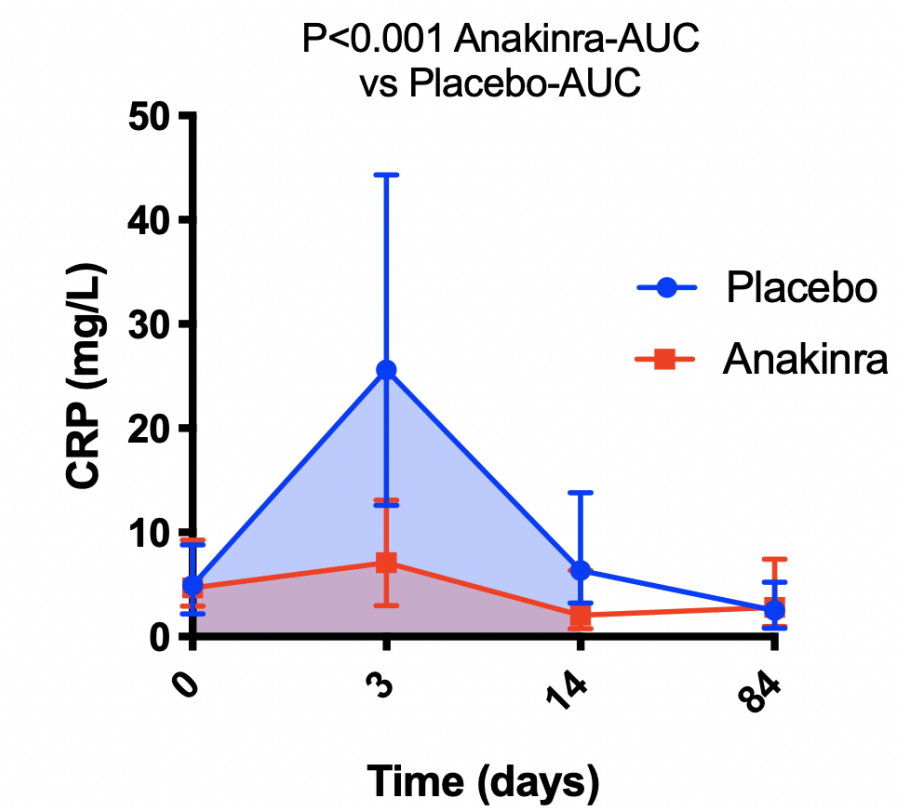
Trial Pooled Cohort



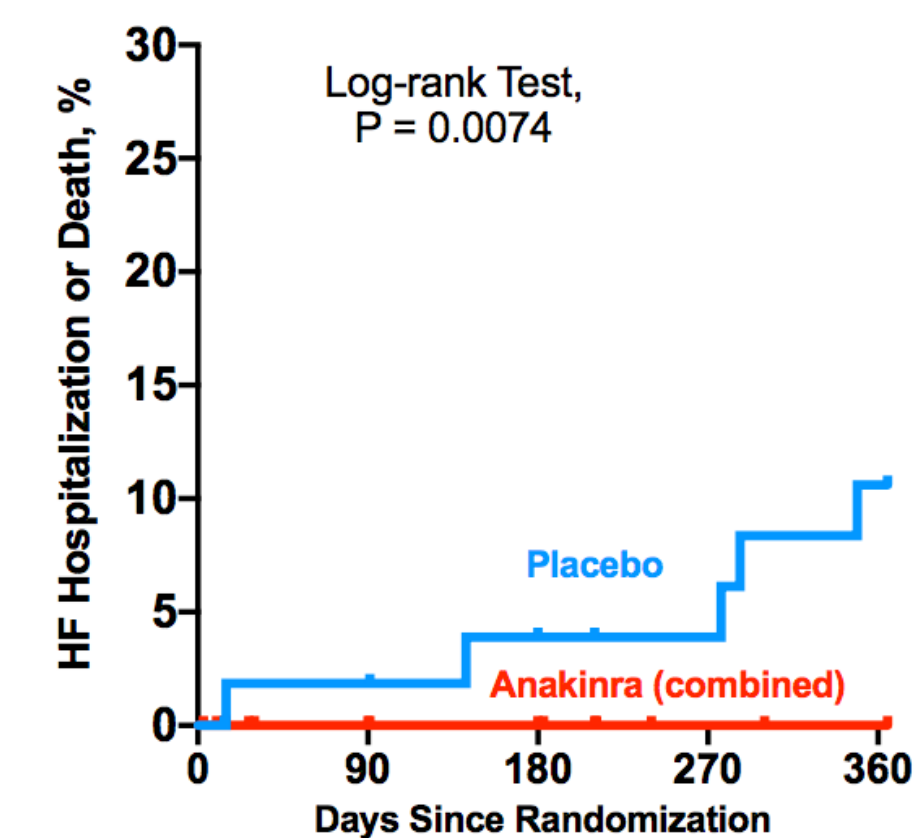
Results: Participants

Baseline Characteristics	Anakinra (n = 84)	Placebo (n = 55)
Age, years (IQR)	55 (48, 61)	57 (51, 65)
Female sex, n (%)	22 (26)	7 (12.7)
Black, n (%)	32 (38.1)	20 (36.4)
Systolic blood pressure, mmHg (IQR)	136 (117, 149)	136 (118, 154)
Diastolic blood pressure, mmHg (IQR)	82 (72, 93)	83 (71, 94)
Heart rate, bpm (IQR)	83 (68, 92)	77 (67, 87)
Symptom to PCI (minutes)	173 (106, 334)	180 (112, 360)
Symptom to Drug (minutes)	509 (359, 741)	502 (383, 681)
C-reactive Protein, mg/L (IQR)	4.7 (2.9, 9.3)	4.95 (2.2, 8.8)
Past Medical History		
Hypertension	45 (54)	37 (67)
Hyperlipidemia	46 (55)	25 (46)
Diabetes	20 (24)	19 (35)
Medications		
ACE-inhibitor/ARB, n (%)	21 (25)	14 (26)
Aspirin, n (%)	25 (30)	14 (26)
Beta-blocker, n (%)	21 (25)	9 (16)
Statin, n (%)	27 (32)	16 (29)
Mineralocorticoid receptor antagonist, n (%)	2 (2.4)	0 (0)
Biguanides, n (%)	8 (10)	11 (20)
Insulin, n (%)	6 (7)	7 (12)
Loop diuretic, n (%)	0 (0)	0 (0)

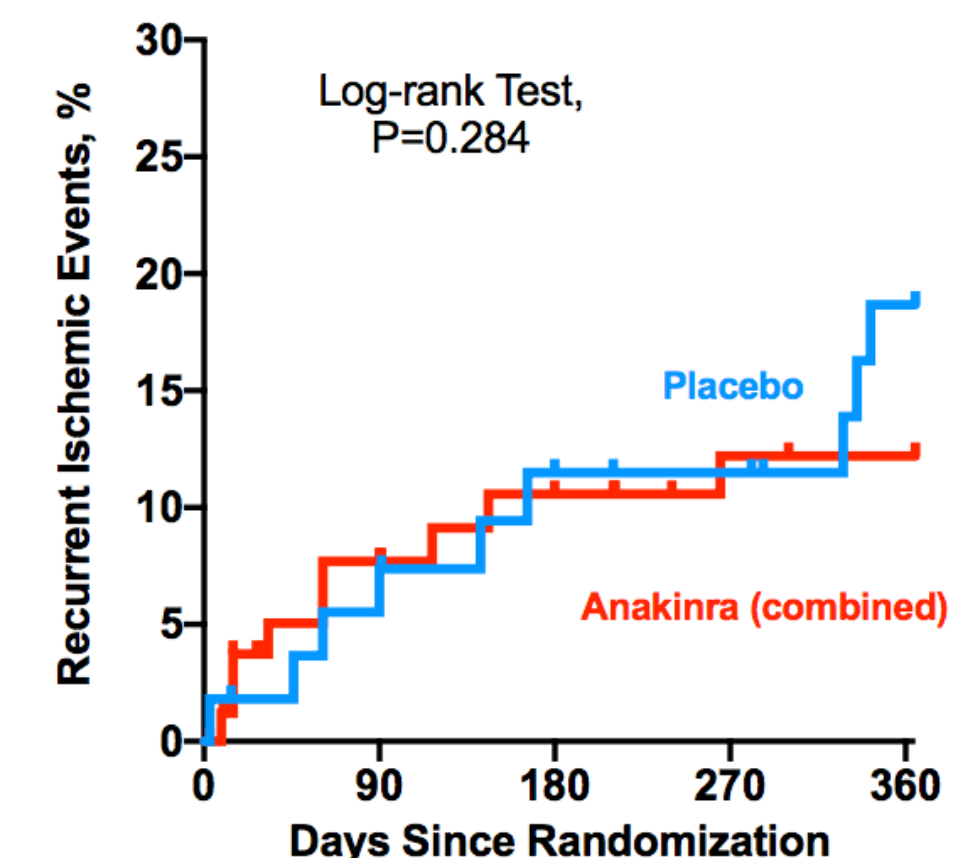
Results: hsCRP AUC₀₋₁₄



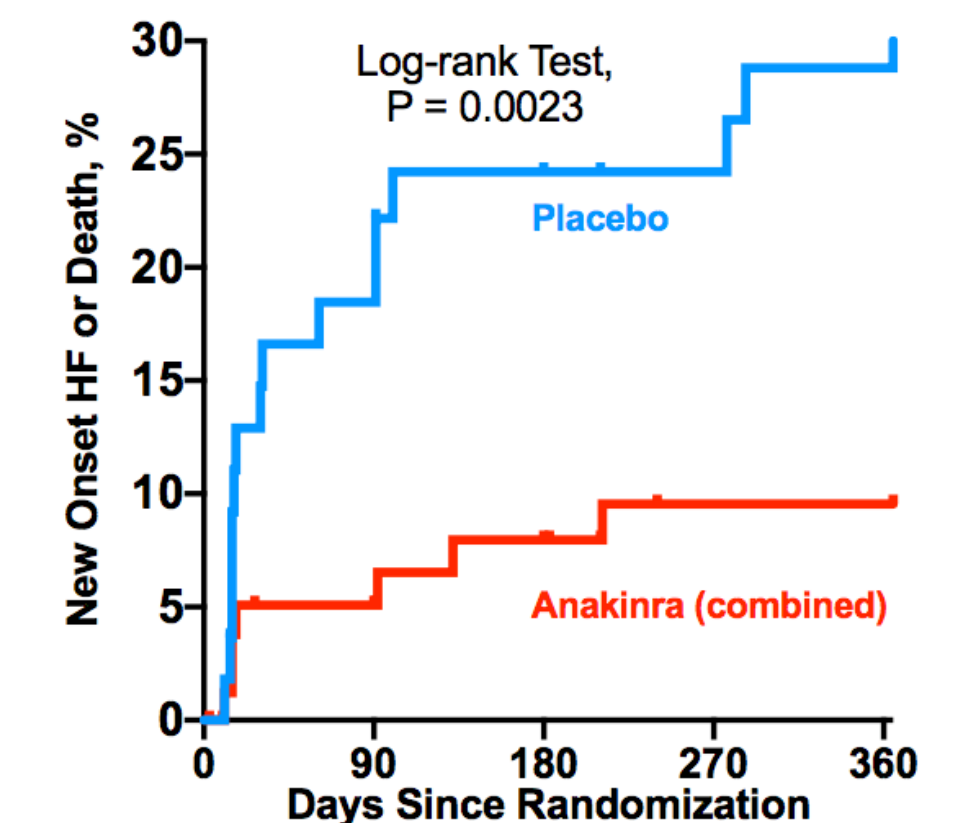
Results: HF Hospitalization or Death



Results: Recurrent Ischemic Event



Results: New Onset HF or Death



Conclusions

- Treatment with anakinra for 14 days following STEMI blunts the inflammatory response (measured as area under the curve for CRP)
- The CRP AUC₀₋₁₄ has independent prognostic value for in-hospital mortality and long-term incidence of HF for patients with STEMI
- Treatment with Anakinra also reduced the occurrence of significant HF events at one year of follow-up
- The benefit seen for new onset HF remains consistent for each of the included studies
- Early and targeted modification of the inflammatory response in STEMI is a safe and effective strategy to improve patient outcomes

References, Disclosures, Financial Support

ClinicalTrials.gov: [NCT00789724](https://clinicaltrials.gov/ct2/show/study/NCT00789724), [NCT01175018](https://clinicaltrials.gov/ct2/show/study/NCT01175018), and [NCT01950299](https://clinicaltrials.gov/ct2/show/study/NCT01950299).
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Please forward question to Dinesh Kadariya at dinesh.kadariya@vcuhealth.org