

Clinical and Quality of Life Outcomes Across the Spectrum of Baseline Kidney Function

Insights from the ISCHEMIA and ISCHEMIA-CKD Trials

Funded by the National Heart, Lung, and Blood Institute

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On behalf of the ISCHEMIA/ISCHEMIA-CKD Research Group

Disclosures

- ISCHEMIA/ISCHEMIA-CKD trials were supported by grants from the NHLBI
- Devices used in the trial were donated by Abbott Vascular, Medtronic, St. Jude Medical, Volcano, and Omron Healthcare; medications were provided by Arbor Pharmaceuticals, AstraZeneca Pharmaceuticals, and Merck Sharp & Dohme.

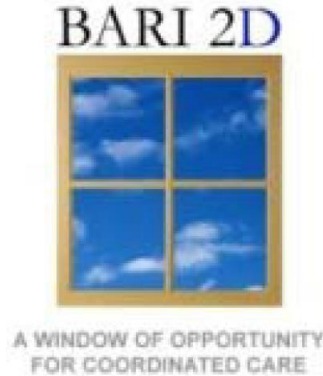
CKD Patients are Under-Represented in Contemporary Revascularization vs. Medicine SIHD Trials

2007



eGFR <30: **16** Subjects

2009



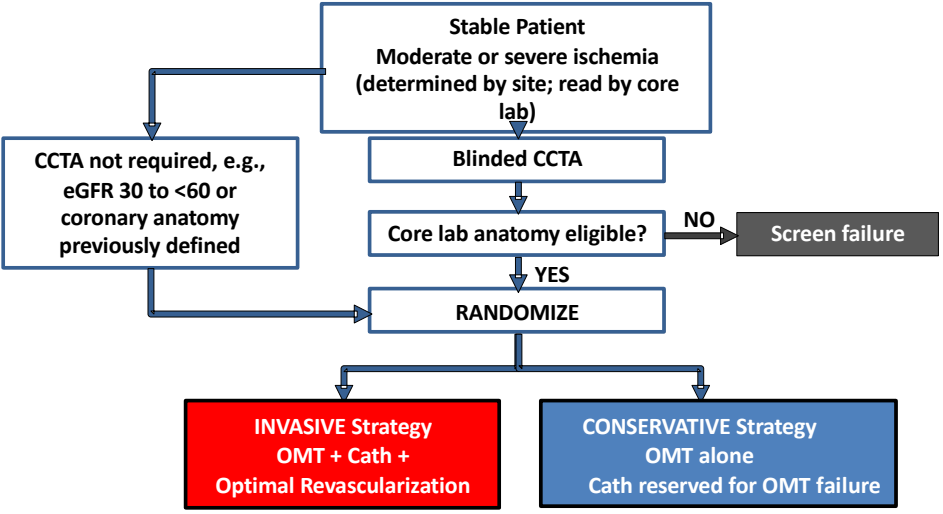
Subjects with serum Cr >2 mg/dl **excluded**

2012

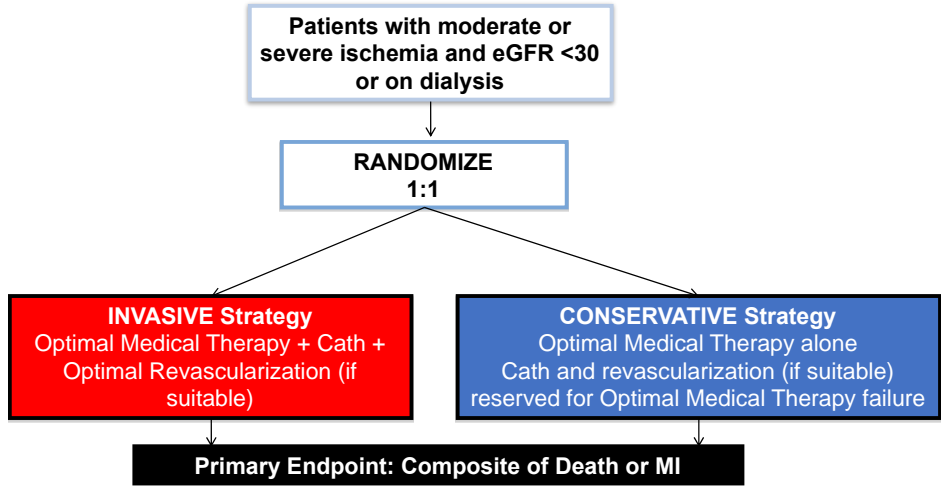
FAME 2 Trial

Serum Cr >2 mg/dl: **20** subjects

Study Design

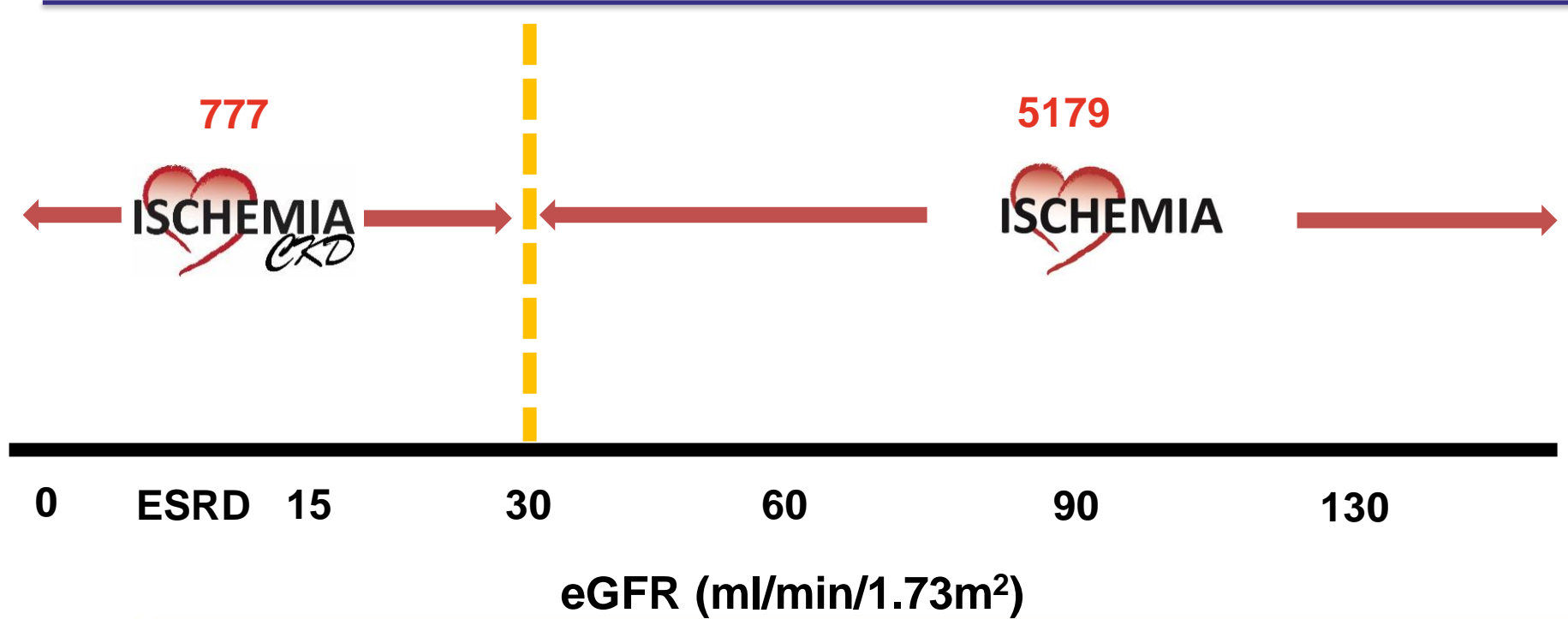


Maron DJ, et al. Am Heart J. 2018; 201;124-135.



Bangalore S, et al. Am Heart J. 2018; 205:42-52

Study Design



Study Objectives

- Evaluate clinical and QoL outcomes across the spectrum of eGFR
- Evaluate the impact of treatment strategy on clinical and QoL outcomes across the spectrum of eGFR

Endpoints

Primary Endpoint

- Time to death or MI

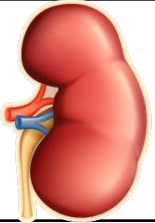
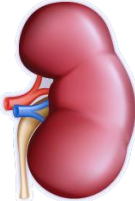
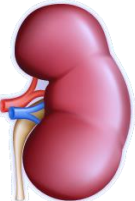


Major Secondary Endpoints

- Time to Death, MI, Hospitalization for Unstable Angina, Heart Failure or Resuscitated Cardiac Arrest
- Quality of Life

Safety Outcomes

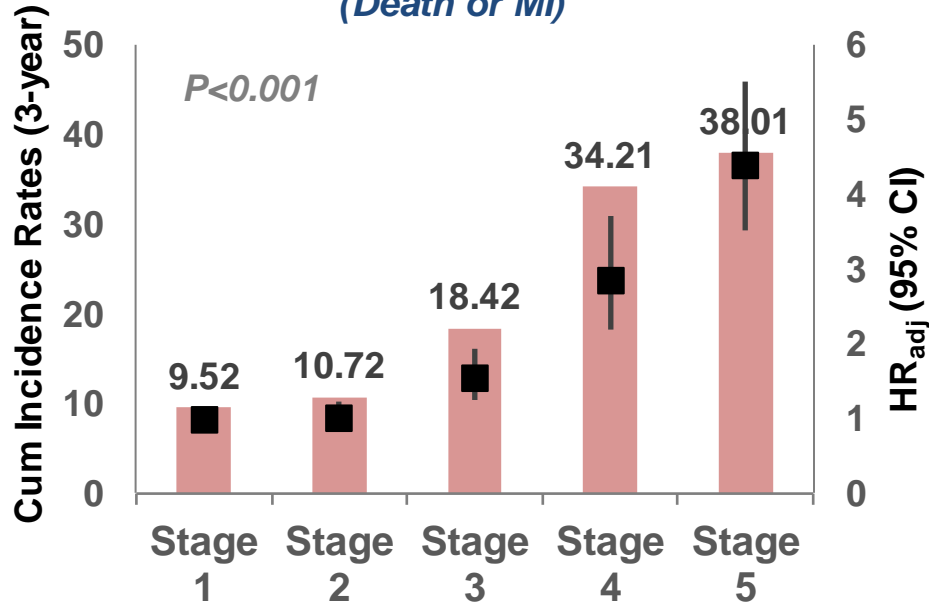
- Procedural complications
- Composite of initiation of dialysis or death

Randomized Participants

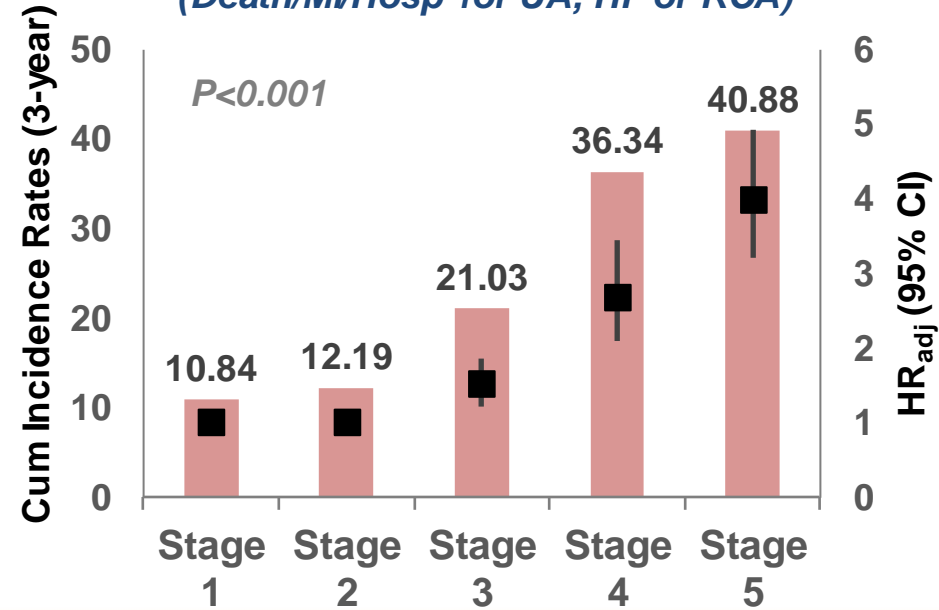
Stage 1 N=1889	Stage 2 N=2551	Stage 3 N=738	Stage 4 N=311	Stage 5/Dialysis N=467
eGFR ≥ 90	90 > eGFR ≥ 60	60 > eGFR ≥ 30	30 > eGFR ≥ 15	eGFR < 15
				
Normal or high function	Mildly reduced function	Moderately reduced function	Severely reduced function	Kidney failure

CKD Stages and Outcomes

Primary Endpoint (Death or MI)



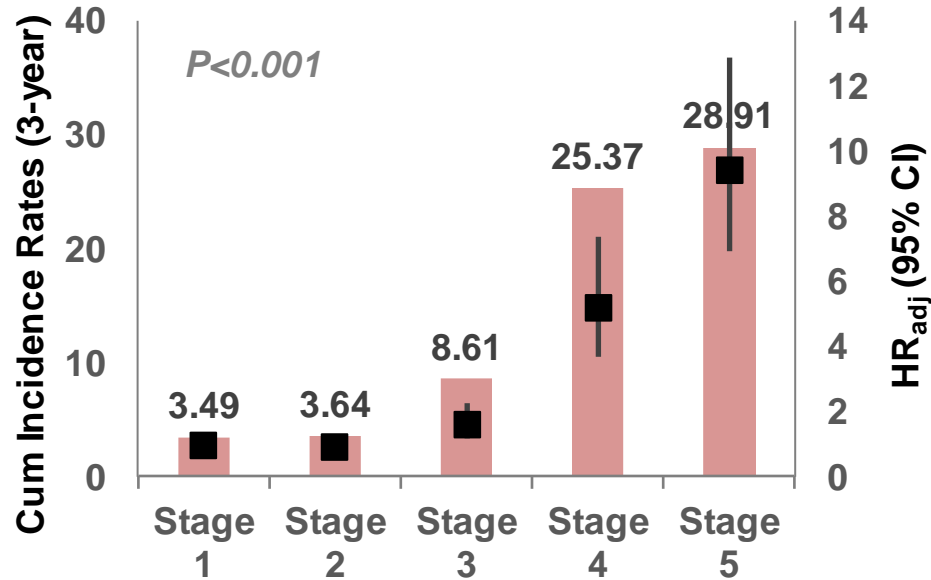
Major Secondary Endpoint (Death/MI/Hosp for UA, HF or RCA)



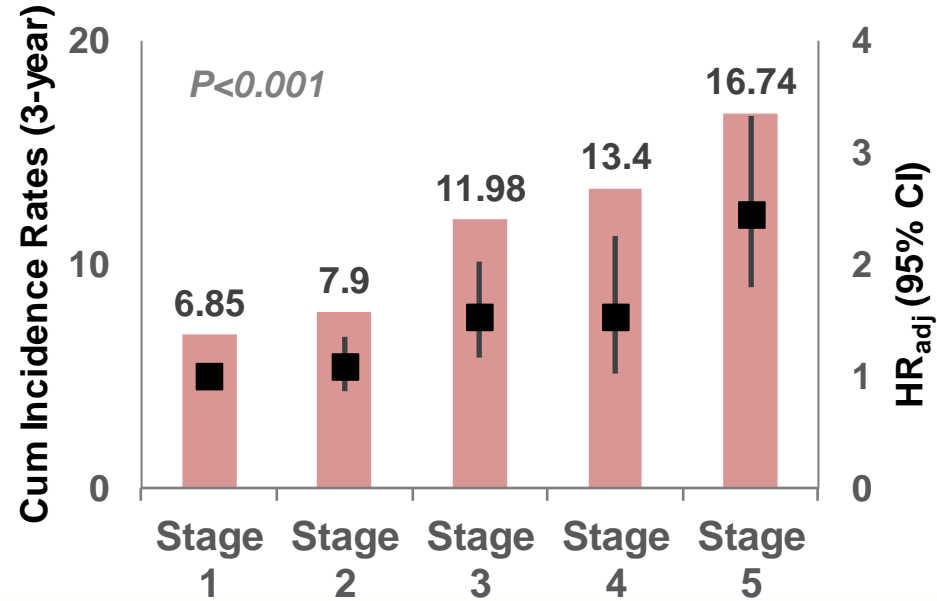
Bars represents cumulative incidence rates and the black squares represents hazard ratio

CKD Stages and Outcomes

All-Cause Death

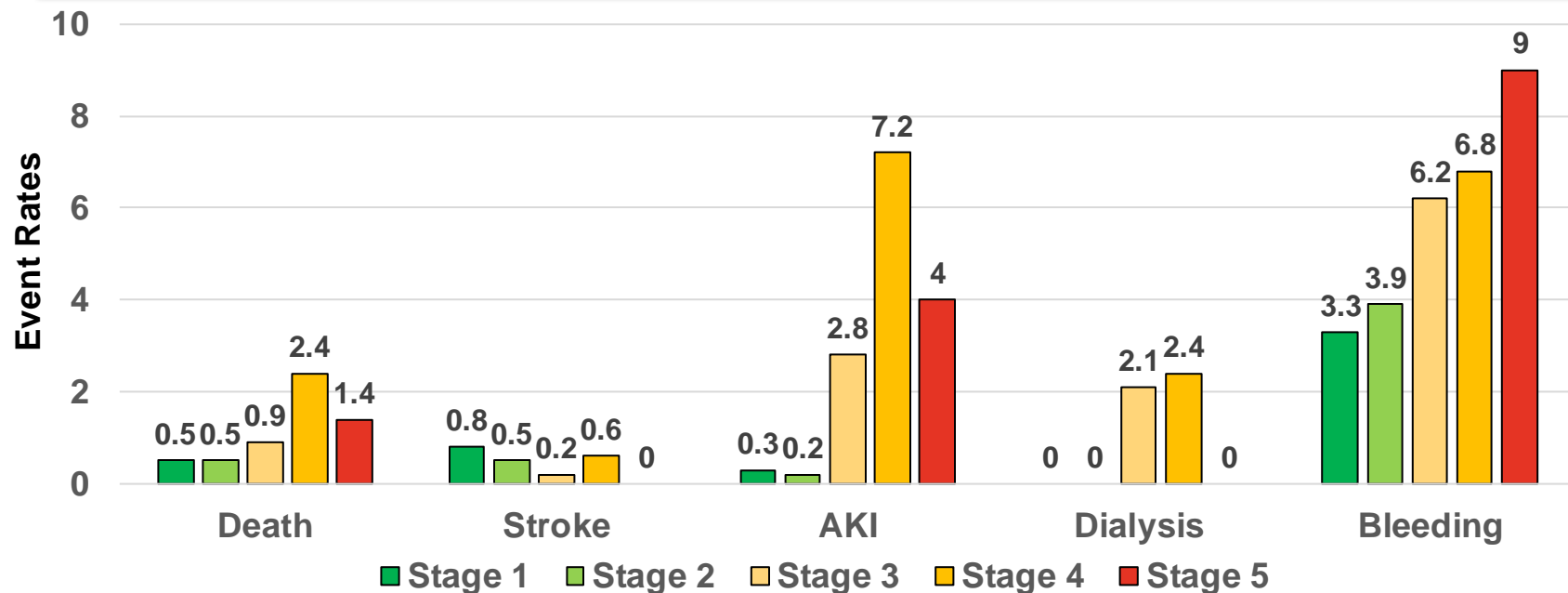


Myocardial Infarction



Bars represents cumulative incidence rates and the black squares represents hazard ratio

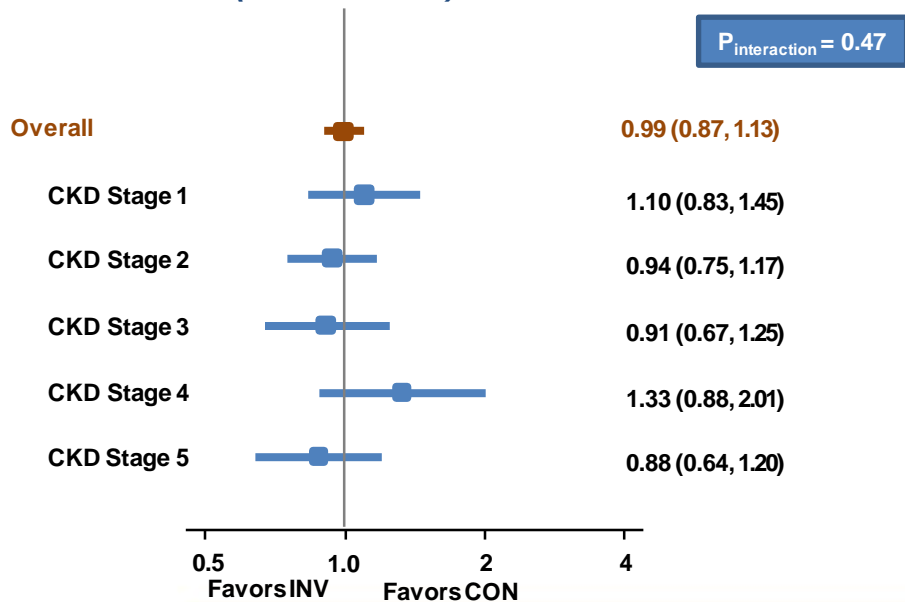
CKD Stages: Procedural Complications and Bleeding



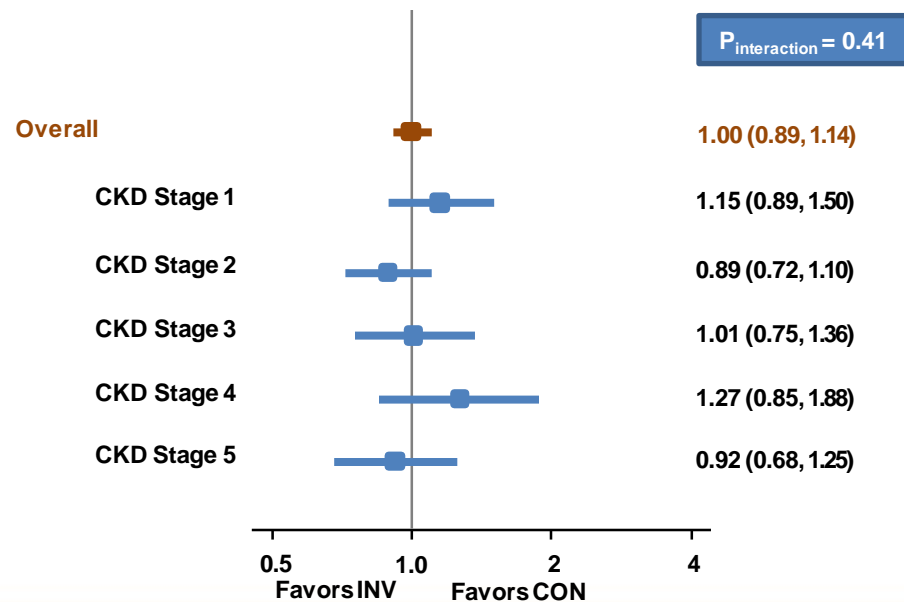
Data are for both INV/CON groups combined. Bleeding outcome for the duration of the trial.

CKD Stages: Heterogeneity of Treatment Effect

Primary Endpoint (Death or MI)

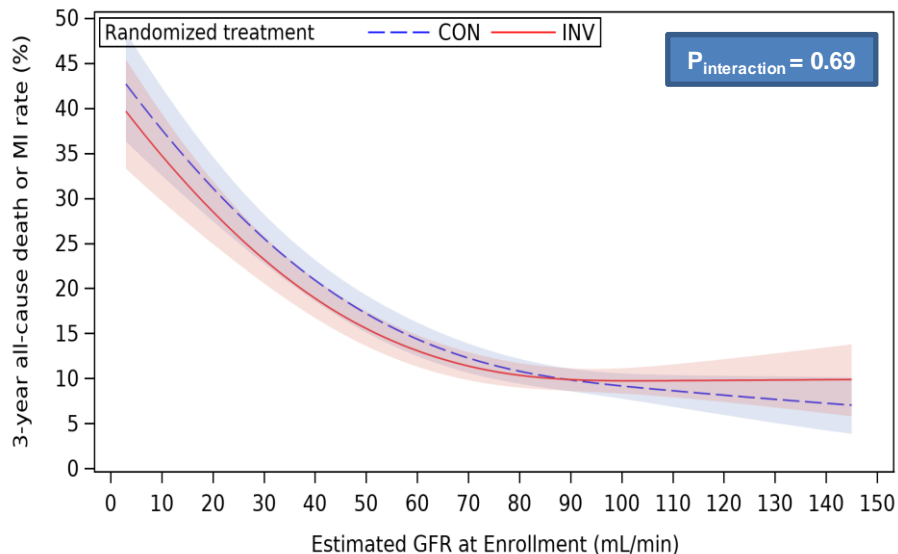


Major Secondary Endpoint (Death/MI/Hosp for UA, HF or RCA)

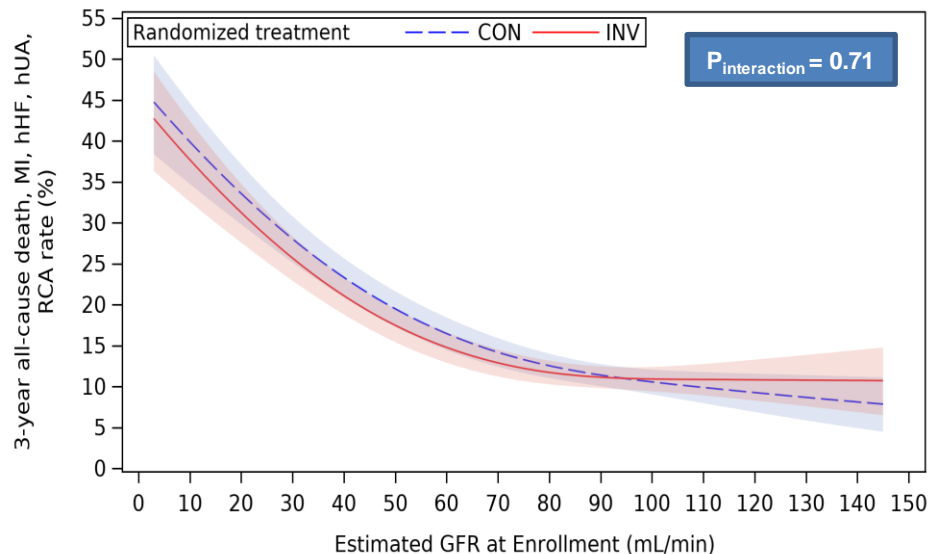


Heterogeneity of Treatment Effect as a Function of eGFR

Primary Endpoint (Death or MI)

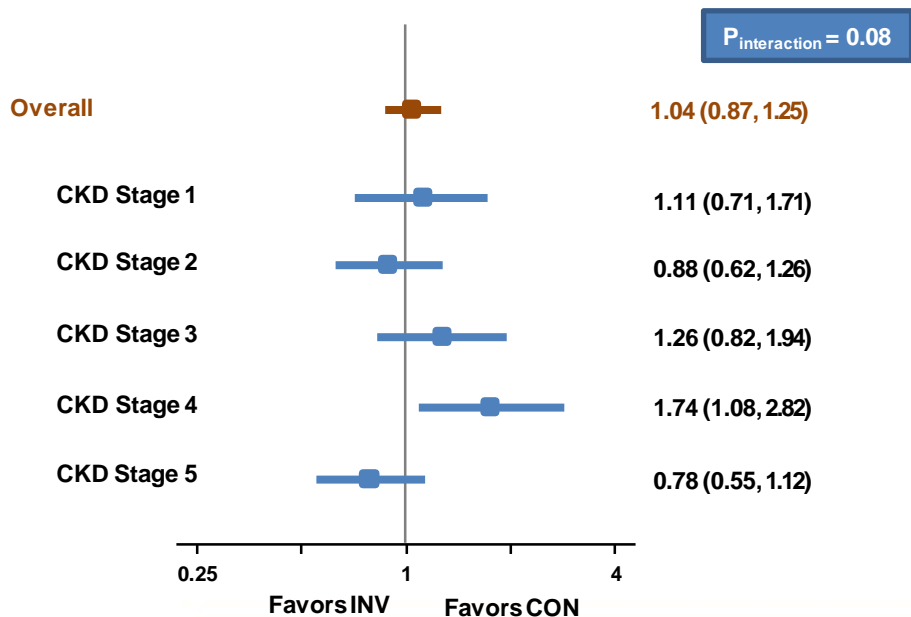


Major Secondary Endpoint (Death/MI/Hosp for UA, HF or RCA)

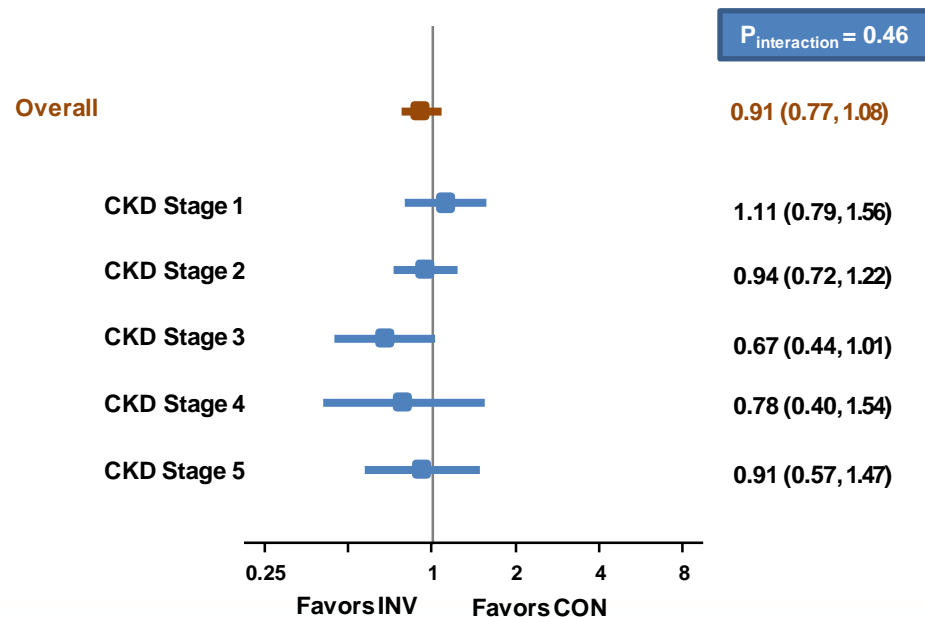


CKD Stages: Heterogeneity of Treatment Effect

All-Cause Death



Myocardial Infarction



CKD Stages: Heterogeneity of Treatment Effect

Procedural MI

$P_{\text{interaction}} = 0.74$

Overall

2.83 (1.83, 4.36)

CKD Stage 1

2.49 (1.10, 5.66)

CKD Stage 2

3.89 (1.99, 7.58)

CKD Stage 3

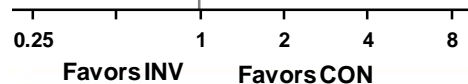
1.87 (0.64, 5.48)

CKD Stage 4

1.93 (0.18, 21.36)

CKD Stage 5

1.84 (0.44, 7.68)



Non Procedural MI

$P_{\text{interaction}} = 0.79$

Overall

0.68 (0.56, 0.83)

CKD Stage 1

0.79 (0.53, 1.17)

CKD Stage 2

0.63 (0.45, 0.88)

CKD Stage 3

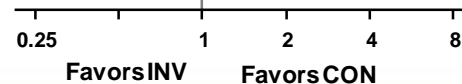
0.59 (0.38, 0.93)

CKD Stage 4

0.61 (0.29, 1.30)

CKD Stage 5

0.82 (0.49, 1.37)



CKD Stages: Heterogeneity of Treatment Effect

Stroke

$P_{\text{interaction}} = 0.08$

Overall

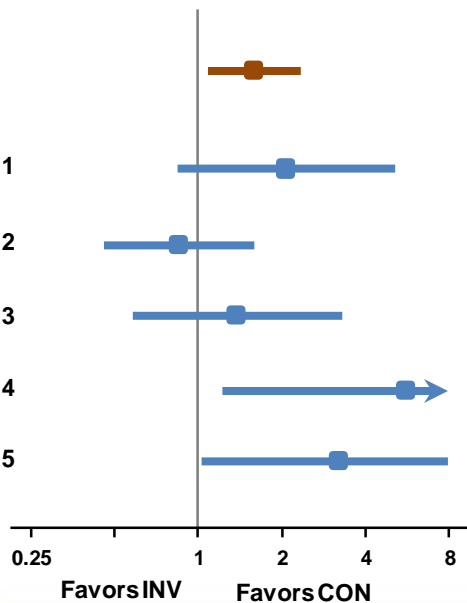
CKD Stage 1

CKD Stage 2

CKD Stage 3

CKD Stage 4

CKD Stage 5



Death or New Dialysis

$P_{\text{interaction}} = 0.29$

Overall

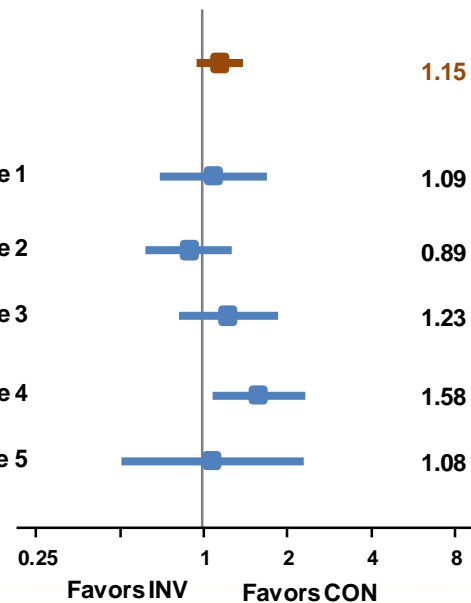
CKD Stage 1

CKD Stage 2

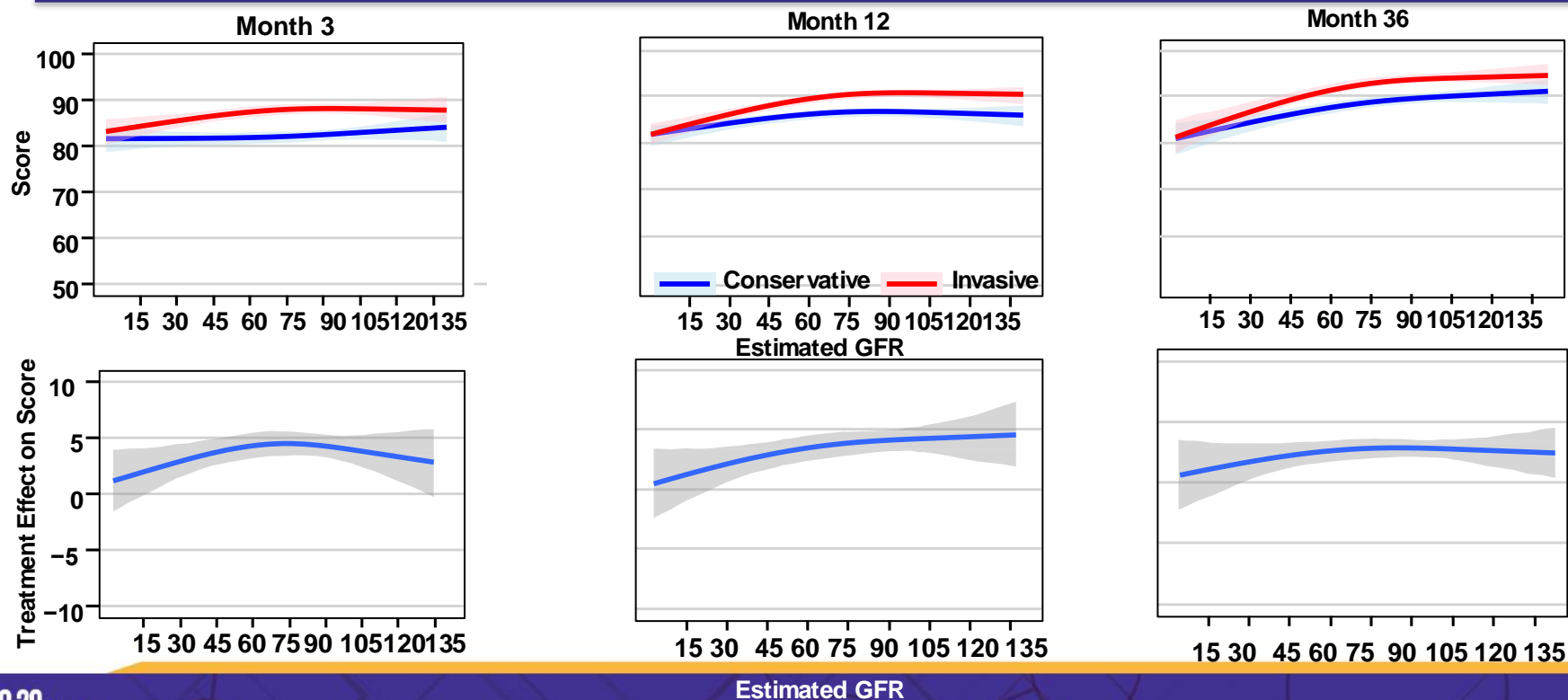
CKD Stage 3

CKD Stage 4

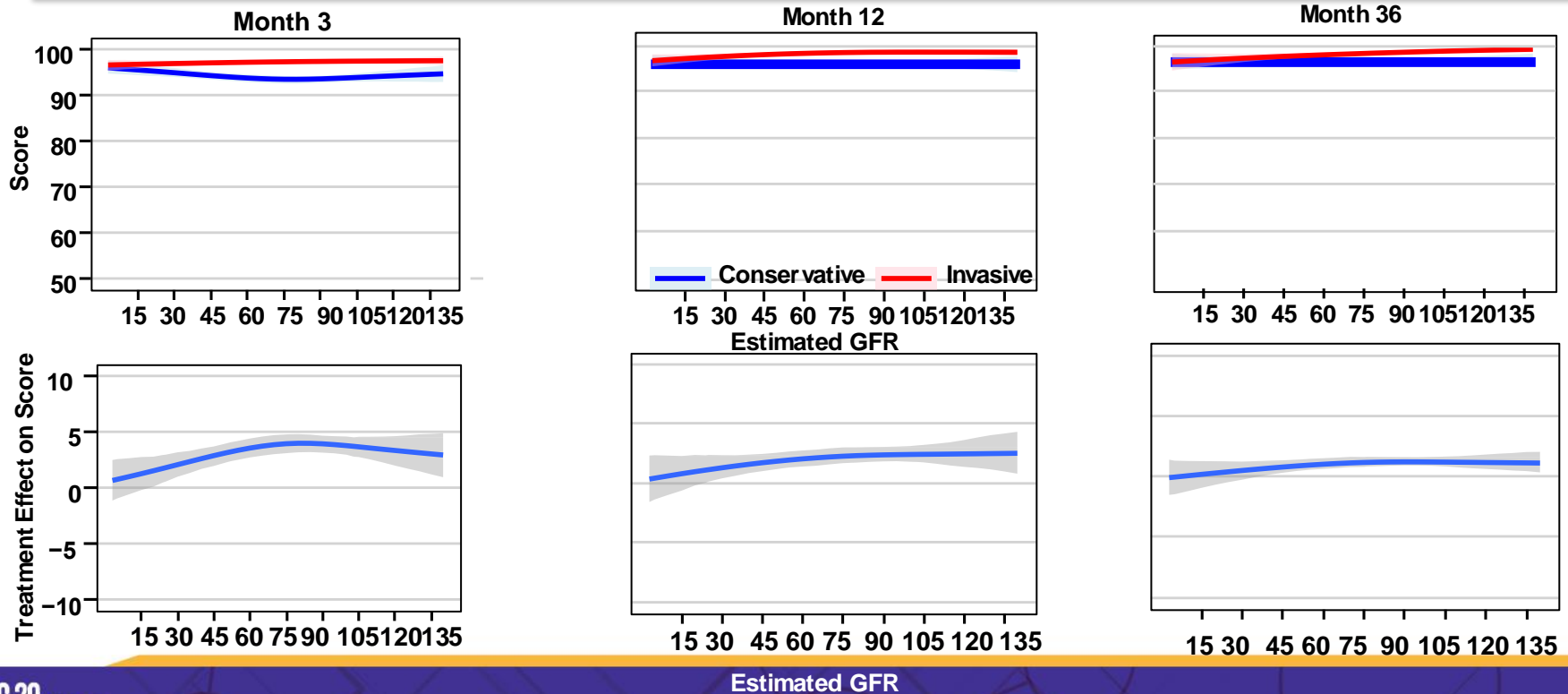
CKD Stage 5



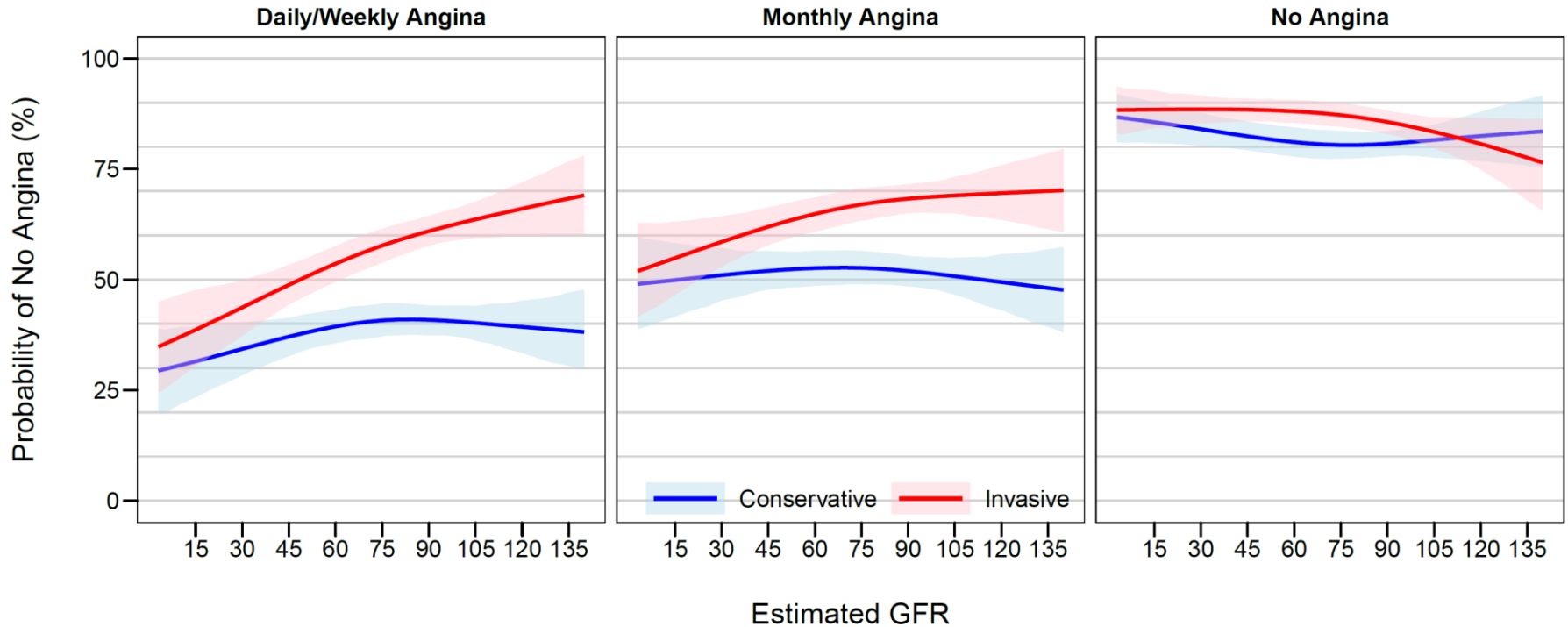
SAQ-7 Summary Score as a Function of eGFR



SAQ-7 Angina Frequency Score as a Function of eGFR



SAQ-7 Angina Frequency Score at 12 months by Baseline Angina Frequency



Conclusions

- Exponential increase in cardiovascular events with lower kidney function
- Procedure related complications and bleeding increased with lower kidney function
- There was no evidence of meaningful heterogeneity of treatment effect for clinical outcomes across eGFR spectrum
 - No difference in INV vs. CON for primary or major secondary outcome
 - Increase in procedural MI but decrease in non procedural MI with INV

Conclusions

- Nominal heterogeneity of treatment effect such that there was
 - Increased risk of death with INV in those with CKD stage 4
 - Increased risk of stroke with INV in those with CKD stage 4/5
- Significant and durable benefit of INV at improving angina related QoL but the effect attenuated in those with less symptoms and at lower eGFR (below 30-45)