

Combining High-Sensitivity Troponin with the AHA/ACC Cholesterol Guidelines To Guide Evolocumab Therapy

Nicholas A. Marston, MD, MPH, Kazuma Oyama, MD, PhD, Petr Jarolim, MD, PhD, Minao Tang, MS, Peter S. Sever, PhD, FRCP, Anthony C. Keech, MD, Armando Lira Pineda, MD, Huei Wang, PhD, Robert P. Giugliano, MD, SM, Marc S. Sabatine, MD, MPH, David A. Morrow, MD, MPH



**Insights into Plaque Vulnerability,
Stabilization and Mechanisms of Death
in Stable Coronary Artery Disease
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Disclosures

Presenter: clinical trial involvement with Amgen, Pfizer, Novartis, and AstraZeneca without personal fees, payments, or salary increase.

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Background

- **Amongst patients with established ASCVD, the 2018 AHA/ACC cholesterol guidelines only recommend PCSK9 inhibitors in patients with *very high-risk* ASCVD.**
- **We have previously shown that a strategy of adding high sensitivity troponin (hsTn) to the guideline's ASCVD risk algorithm reclassifies a substantial portion of not very high-risk ASCVD patients into the very-high risk group.**
- **We hypothesized that this reclassified cohort would derive benefit from PCSK9 inhibition, despite not currently carrying a guideline recommendation.**

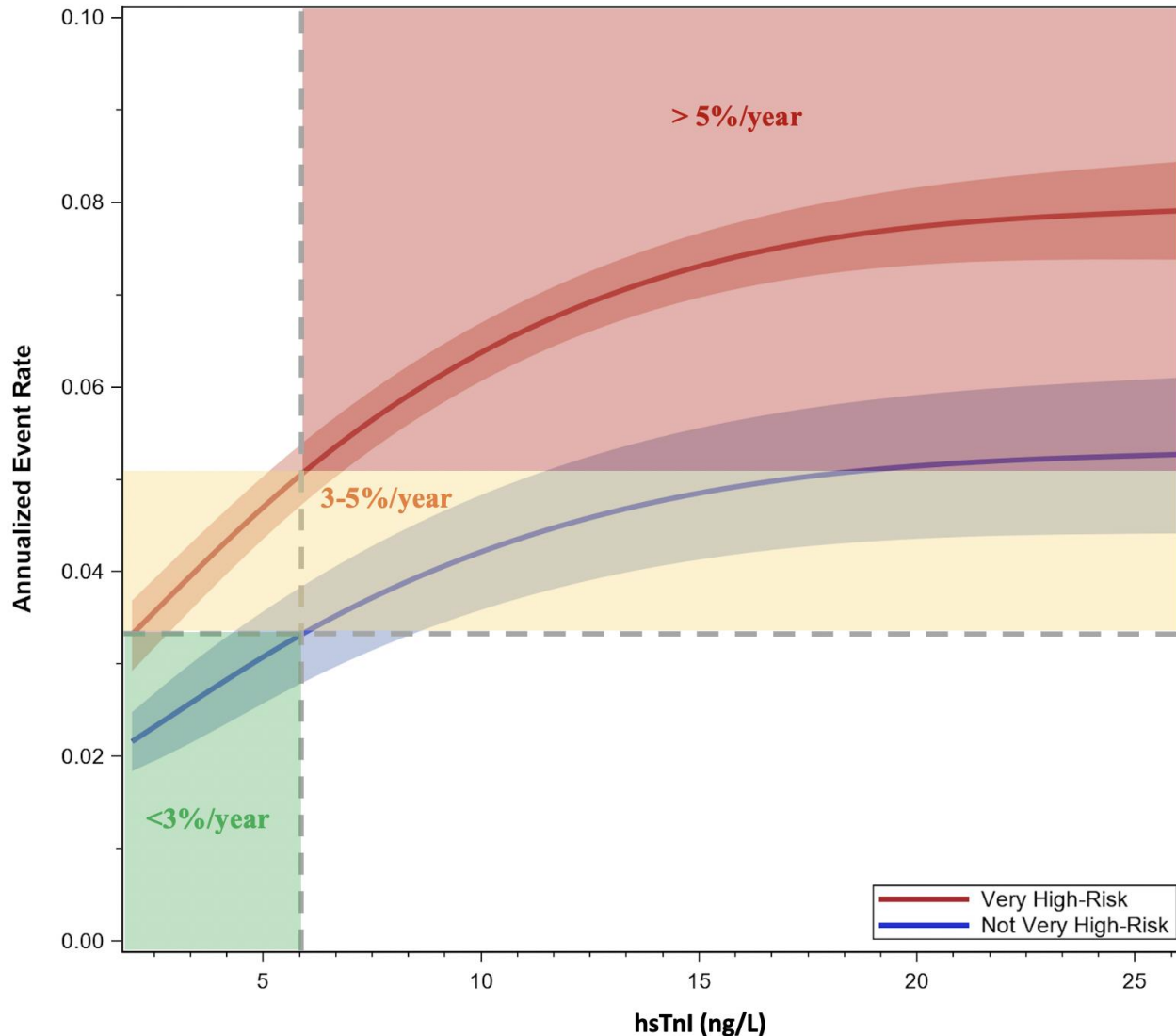
Methods:

- **Prospective cohort analysis within the FOURIER trial, a randomized, placebo-controlled cardiovascular outcomes trial of the PCSK9 inhibitor evolocumab.**
- **Patients were assigned to guideline-based ASCVD risk categories of “very high-risk” or “not very high-risk”, followed by classification based on hsTnI (Abbott ARCHITECT) using an *a priori* risk threshold of 6 ng/L.**
- **Major vascular events were adjudicated with a median follow-up of 2.2 years.**

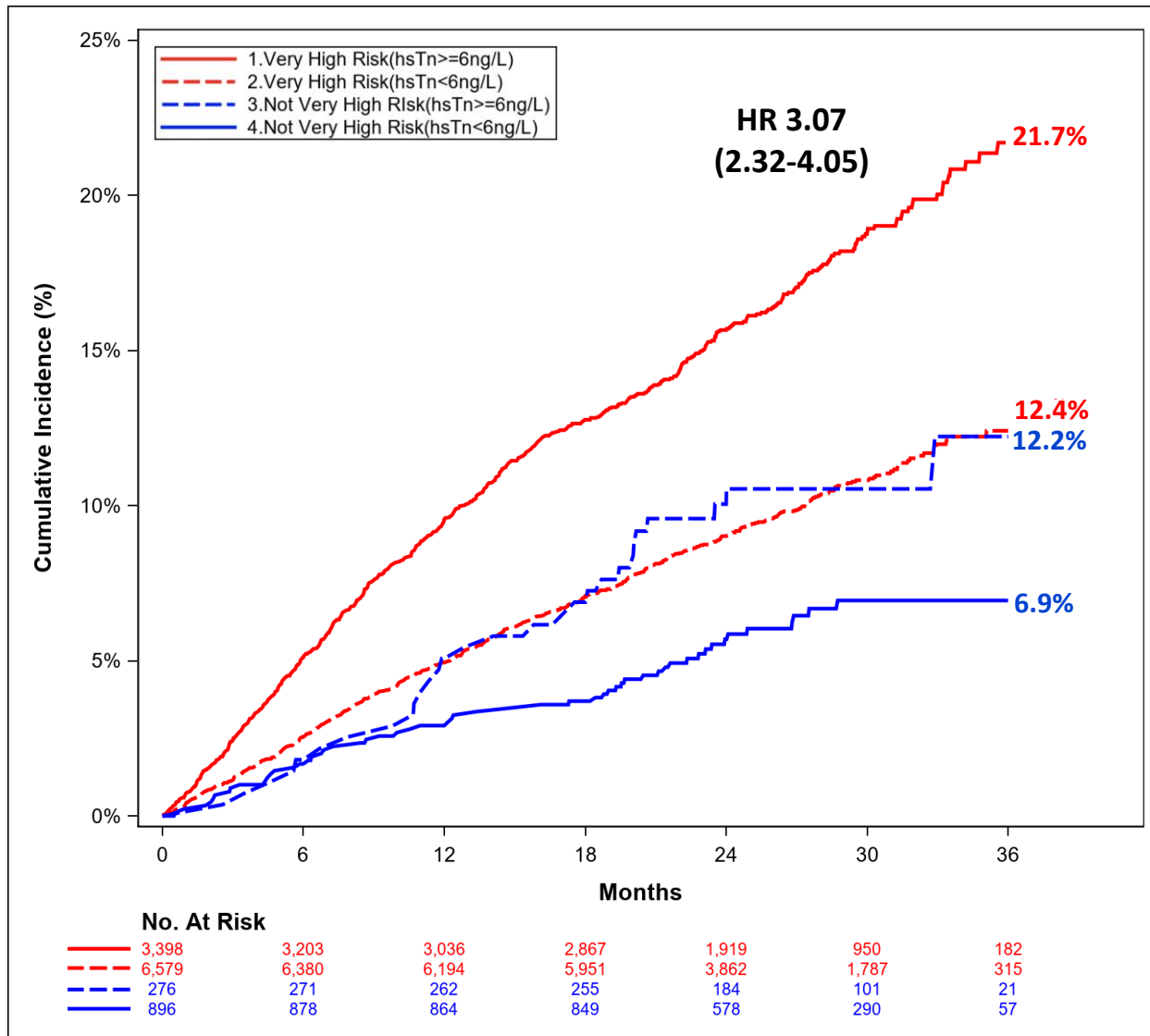
Results: Baseline Characteristics by hsTn

	hsTn < 6 ng/L N= 14,826	hsTn ≥ 6 ng/L N= 7,398	P-value
Demographics, %			
Age ≥ 65	42	52	<0.0001
Female	28	19	<0.0001
Medical History, %			
Prior MI	78	86	<0.0001
Prior Stroke	20	18	<0.0001
Hx of PAD	14	15	0.0226
Prior Coronary Revasc	64	70	<0.0001
Diabetes Mellitus	33	40	<0.0001
Hypertension	79	83	<0.0001
Current Smoker	30	24	<0.0001
LDL-C >100 mg/dl	37	36	0.07
Prior CHF	20	34	<0.0001
Laboratory Values, %			
eGFR <60 mL/min/1.73m ²	15	27	<0.0001

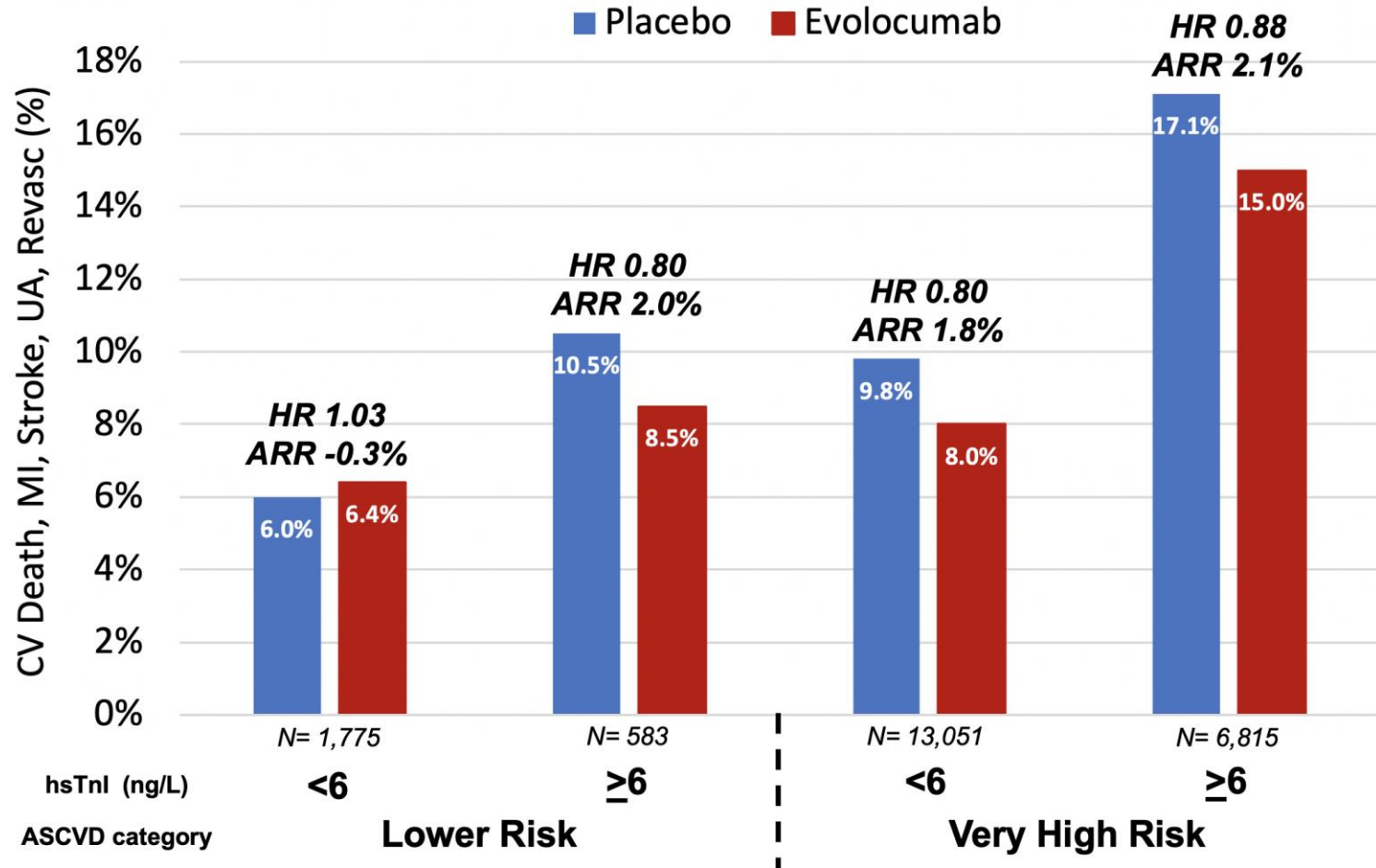
Results: ASCVD Clinical Risk, hsTn, and the Probability of a Major Vascular Event



Results: Major Vascular Events stratified by hsTn + ASCVD clinical risk



Results: Treatment Effect with Evolocumab stratified by hsTnl and ASCVD Risk Category



Limitations

- **Given the entry criteria of the FOURIER trial, the majority of patients in this analysis met criteria for very high-risk ASCVD.**
- **As a result, the proportion of patients with lower-risk ASCVD and hsTn ≥ 6 ng/L, the subgroup of greatest interest, was modest in size.**
- **However, these are the only available data to address the question as to whether hsTn can guide PCSK9 inhibitor therapy for improved outcomes.**
- **The ongoing VESALIUS-CV trial is testing evolocumab in a lower-risk ASCVD population and will provide an additional and larger “not very high-risk” study cohort to assess consistency with our results.**

Conclusions

- **hsTnI identifies a cohort of “not very high-risk” ASCVD patients who are at greater risk than otherwise appreciated**
- **These patients derive absolute and relative risk reductions with evolocumab on par with clinically very high-risk ASCVD patients**