Physiology-guided Complete vs. Culprit-Only Revascularization in Older MI Patients with HBR status: Insights from the

FIRE TRIAL

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CRF TCT

Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a relevant financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	Ineligible Company
Grant/Research Support	Medis, SMT, Siemens, Insight Lifetech, GE
Consultant Fees/Honoraria	SMT, Siemens, Medis, Abbott and Insight Lifetech

All relevant financial relationships have been mitigated.
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Background

- HBR status correlates with an increased risk of bleeding and ischemic complications [1].
- Enhancement of HBR patients outcomes have predominantly centered on identification of HBR status, radial access, optimization of antithrombotic regimens (intensity and length modulation) and selection of new-generation drug-eluting platforms [2].
- The FIRE study population represents a unique opportunity to generate evidence regarding the optimal revascularization strategy for HBR patients [3].

1. Circulation. 2019;140:240-261. 2. Nat Rev Cardiol. 2022;19:117-132. 3. N Engl J Med. 2023:389:889-898.

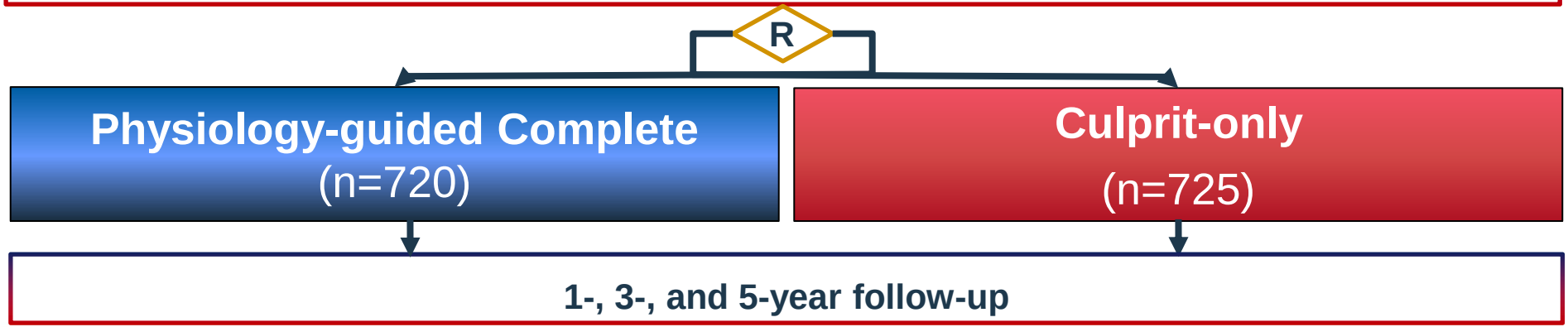
Design

All comers, prospective, randomized, multicenter, open-label trial with blinded adjudicated evaluation of outcomes (PROBE).

Pts ≥75 ys hospitalized for MI (STE or NSTE) with indication to invasive management

Multivessel disease at coronary artery angiography

Culprit lesion clearly identifiable and successfully treated

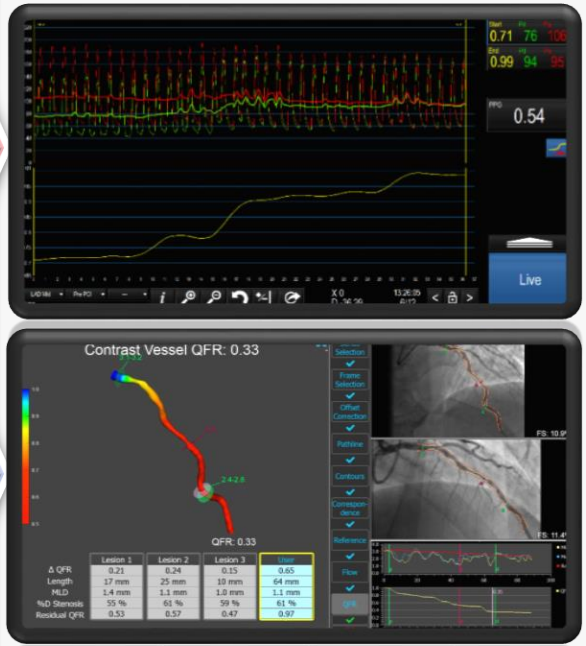


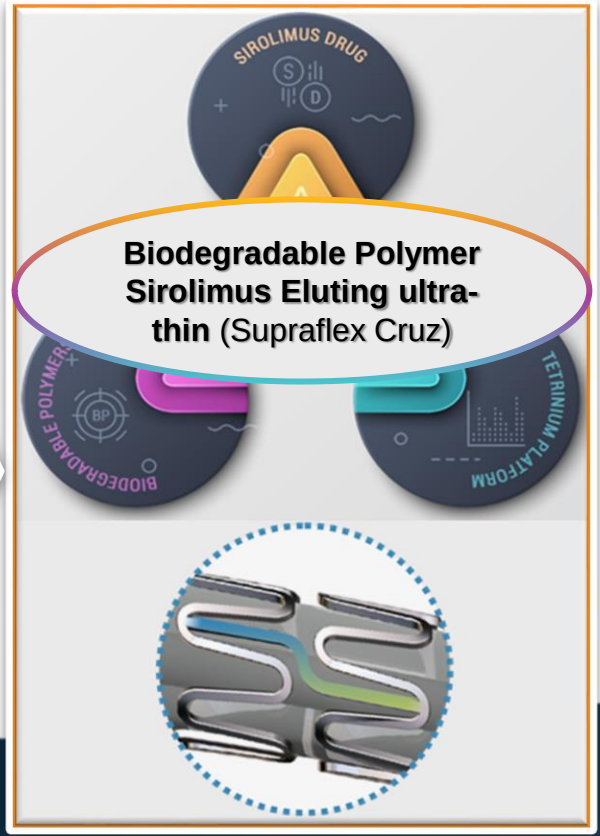
1-, 3-, and 5-year follow-up

Coronary Physiology & Stents

- Non-culprit lesions were assessed with either wire-based FFR, resting index or angiography-derived FFR
- Flow-limiting lesions (FFR≤0.80, resting ≤0.89) had to be revascularized with biodegradable-polymer sirolimus ultra-thin stent(s)

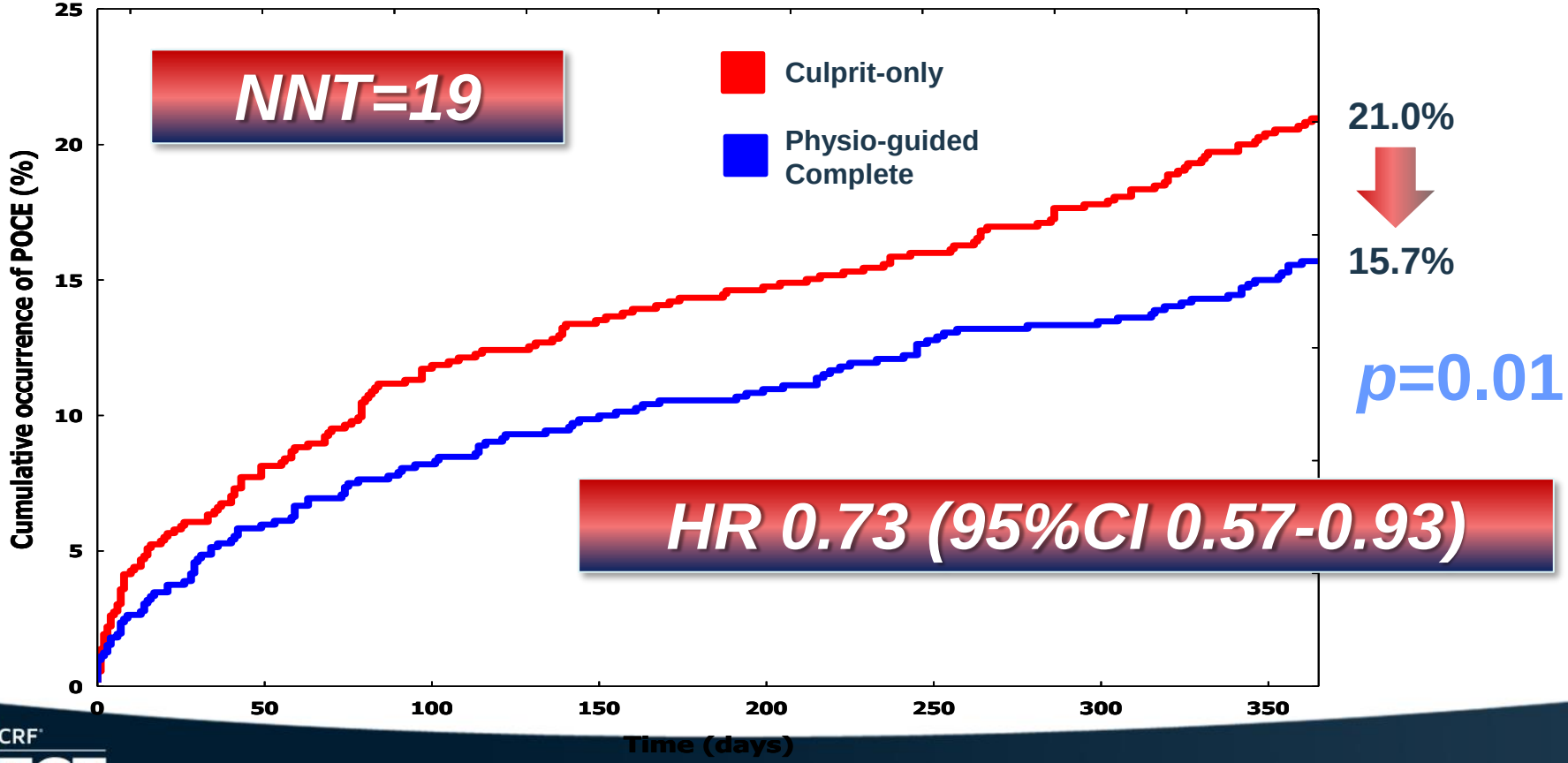
OR





Primary endpoint

All-cause death, any MI, stroke, or ID-revascularization



Biscaglia S, et al. N Engl J Med. 2023 Sep 7;389(10):889-898.

Prespecified HBR analysis - Aims

i. To describe the *prognostic impact* of HBR status

ii. To investigate the efficacy and safety across HBR status of *physiology-guided complete* versus culprit-only strategy

iii. To explore outcomes of HBR patients treated with *≤1 m* vs. >1 m *DAPT* regimen with biodegradable polymer sirolimus eluting ultra-thin stent

Endpoints

Primary

Death, any MI, any stroke, or ID-revascularization

Key secondary

Cardiovascular death or MI

Safety

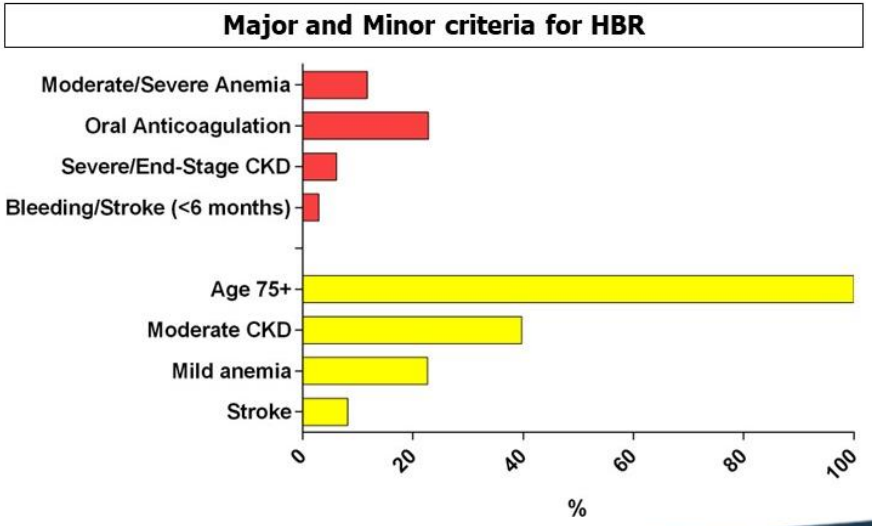
BARC type 3-5 bleeding

Baseline Characteristics

No differences between complete and culprit-only in HBR and non-HBR patients

Characteristic	non-HBR (n=420)	HBR (n=1025)	p
Age – years	79.6±4	81.5±4	<0.001
Female sex	140 (33)	388 (38)	0.118
Medical history			
Hypertension	323 (77)	862 (84)	<0.001
Diabetes	120 (28)	343 (33)	0.089
Prior MI	40 (10)	180 (17)	<0.001
History of AF	4 (1)	196 (19)	<0.001
eGFR<60 ml/min	0 (0)	662 (65)	<0.001
PAD	49 (12)	200 (19)	<0.001
CVA	0 (0)	119 (12)	<0.001
Killip ≥2	75 (18)	337 (33)	<0.001
LVEF – %	51.1±10	48.4±11	<0.001

1025/1445 (71%) fell within the HBR category, as defined by the ARC-HBR criteria



Baseline Characteristics

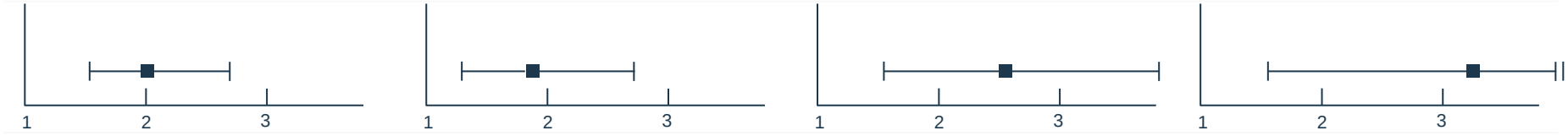
No differences between complete and culprit-only in HBR and non-HBR patients

Characteristic	non-HBR (n=420)	HBR (n=1025)	p
Antithrombotic drugs at discharge – no. (%) *			
Aspirin	419 (99)	956 (93)	<0.001
Clopidogrel	103 (25)	626 (61)	
Ticagrelor	297 (71)	366 (36)	<0.001
Prasugrel	19 (4.5)	13 (1)	
Vitamin K antagonist	0 (0)	63 (6)	<0.001
NOAC	0 (0)	266 (26)	<0.001
DAPT	419 (99)	676 (66)	<0.001
DAT	0 (0)	53 (5)	<0.001
TAT	0 (0)	276 (27)	<0.001

Characteristic	non-HBR (n=420)	HBR (n=1025)	p
Culprit vessel – no. (%)			
LM	8 (2)	68 (7)	
LAD	186 (44)	473 (46)	
LCX	95 (23)	174 (17)	<0.001
RCA	120 (28)	293 (28)	
RI	11 (3)	17 (2)	

Study Endpoints

HBR vs non-HBR patients

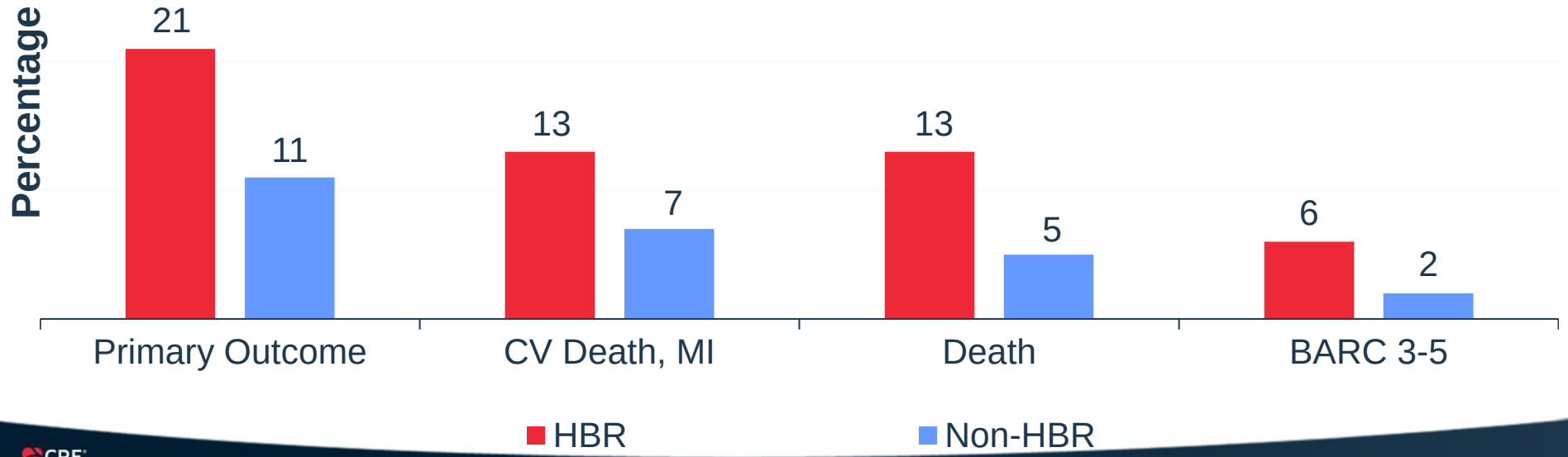


HR 2.01, 95%CI 1.47-2.76, p<0.001

HR 1.89, 95%CI 1.26-2.83, p=0.001

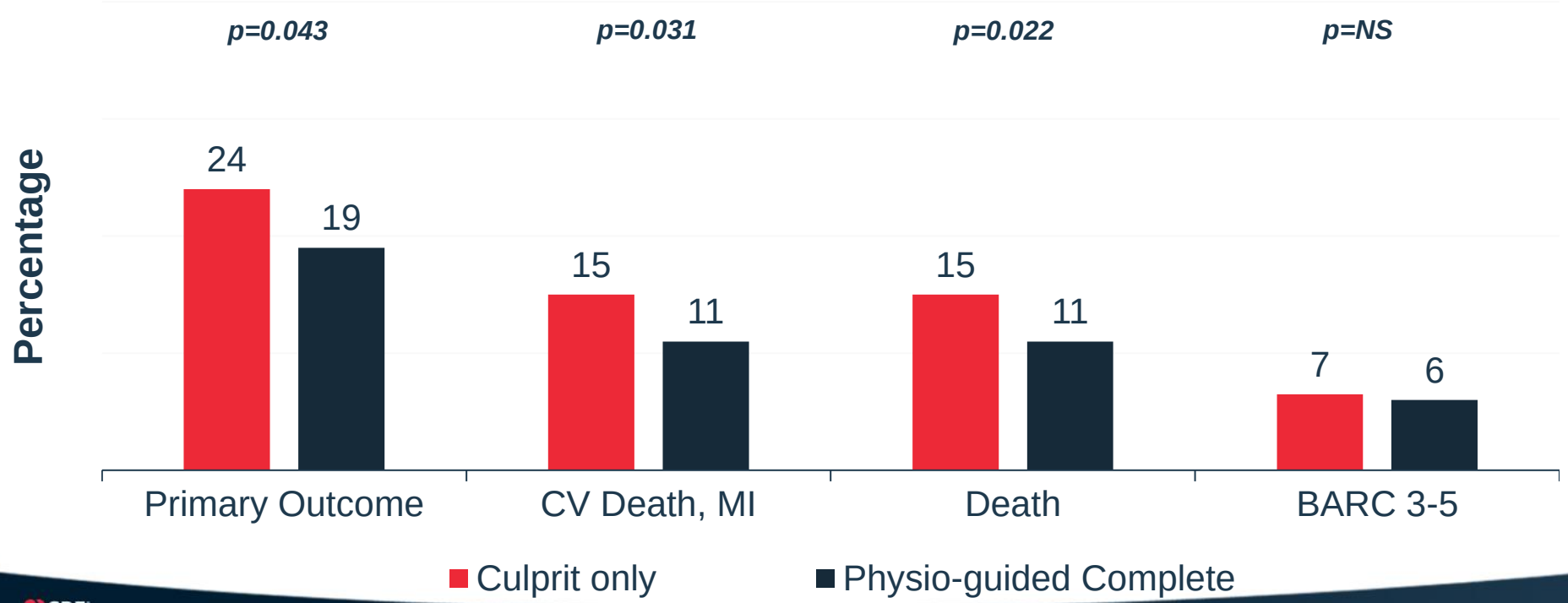
HR 2.53, 95%CI 1.63-3.94, p<0.001

HR 3.28, 95%CI 1.40-7.64, p=0.006

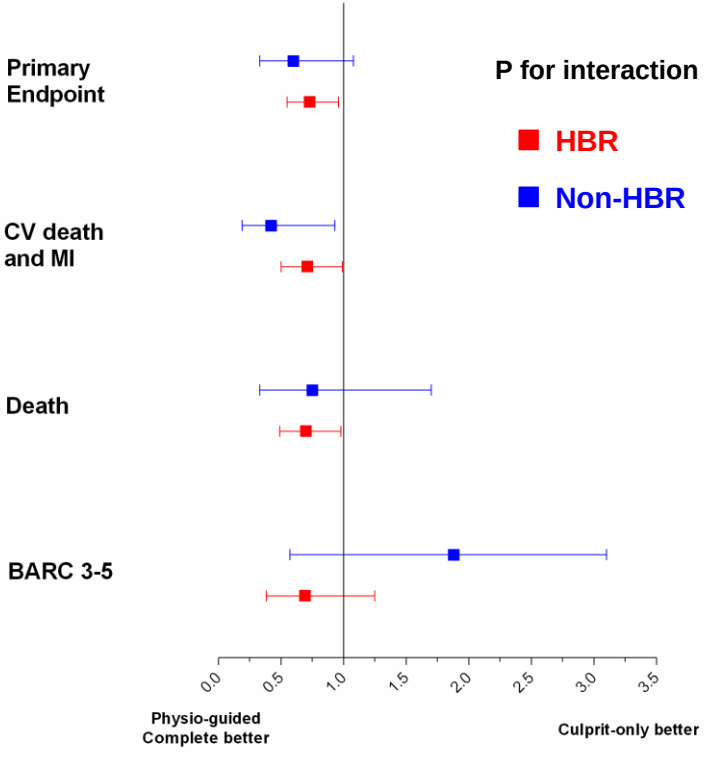


Study Endpoints

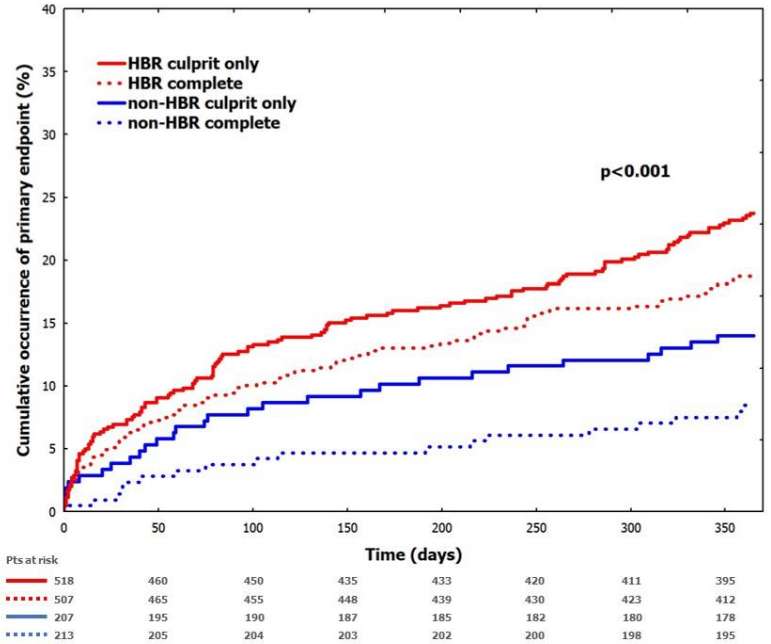
HBR patients / Culprit vs Physio-Complete



HBR vs non-HBR patients

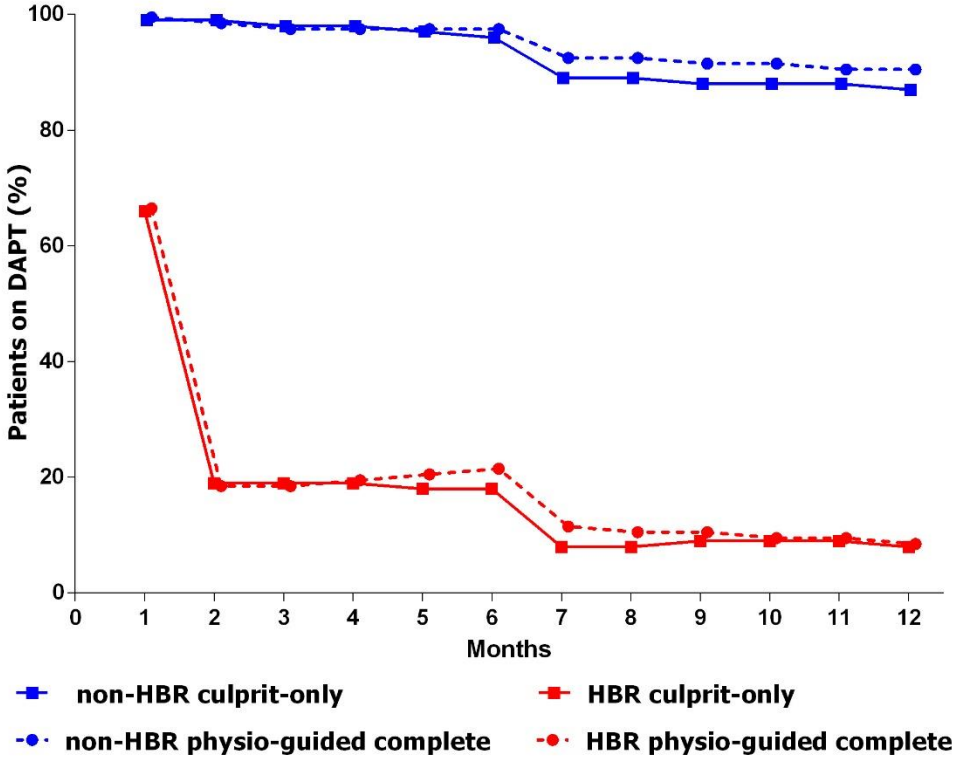


Primary Endpoint



DAPT in HBR patients in the FIRE trial

- In HBR patients DAPT was suggested for one month [1].
- In presence of OAT, the protocol suggested DAT (i.e., clopidogrel plus NOAC).
- If the physician opted for TAT (i.e., aspirin, clopidogrel plus NOAC), such a regimen was recommended for a maximum period of 30 days.

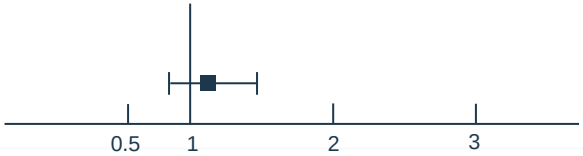


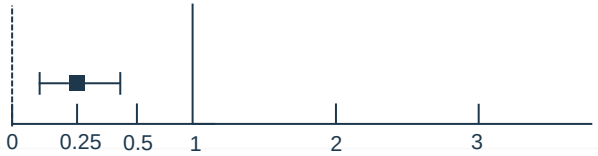
1. Circulation. 2023;147(25):1933-1944

Study Endpoints

DAPT ≤1-month 611 (61%)

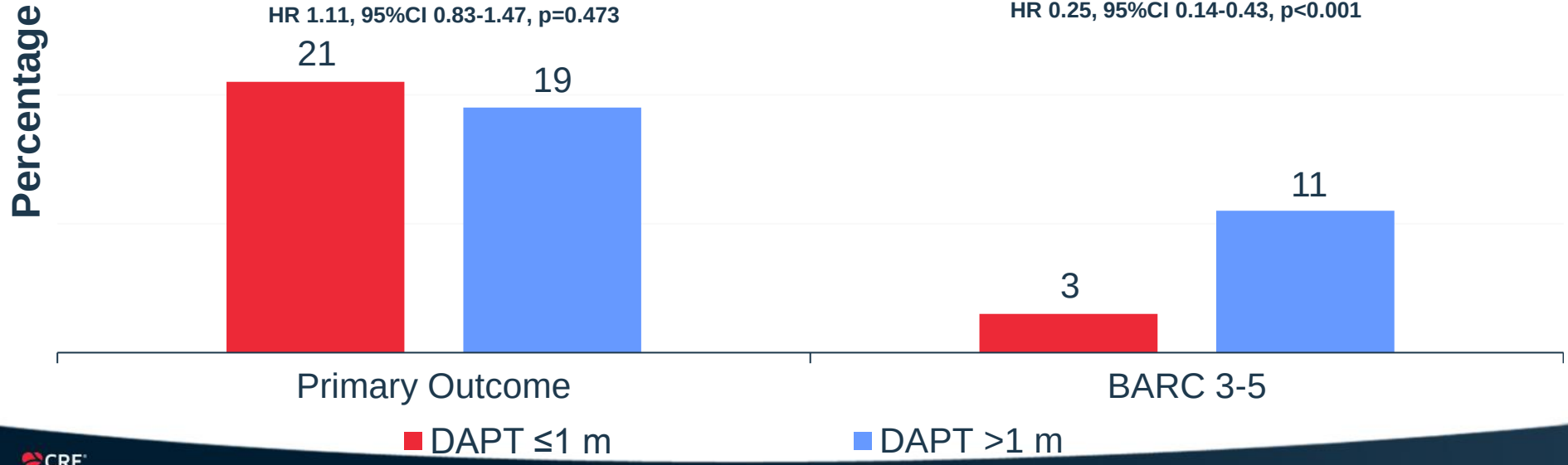
DAPT >1-month 398 (39%)





HR 1.11, 95%CI 0.83-1.47, p=0.473

HR 0.25, 95%CI 0.14-0.43, p<0.001



*The baseline characteristics of these 2 subgroups did not differ except for diabetes that was less frequent in HBR patients treated with DAPT regimen ≤1-month

Limitations

- To investigate the effect of physiology-guided complete revascularization in HBR patients was not the primary aim of the FIRE trial
- Findings on secondary endpoints should be considered with caution
- It remains uncertain whether our study's outcomes can be extrapolated to patients managed with different strategies and stent platforms

Conclusions

1. HBR status *amplifies* the risk of adverse events in a group of older MI patients with MVD
2. In HBR patients *Physio-guided complete* revascularization reduced primary and key secondary endpoint and should be pursued
3. *Short DAPT* regimen was safe regarding ischemic events and effective in major bleeding reduction in HBR patients treated with Supraflex Cruz

FIRE trial – Editorial Comment

Hector M. Garcia-Garcia, MD, PhD

Professor of Medicine, Georgetown University

Washington Hospital Center

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Consultant Fees/Honoraria	Boston Scientific, Abbott, MedAlliance, Medis, ACIST

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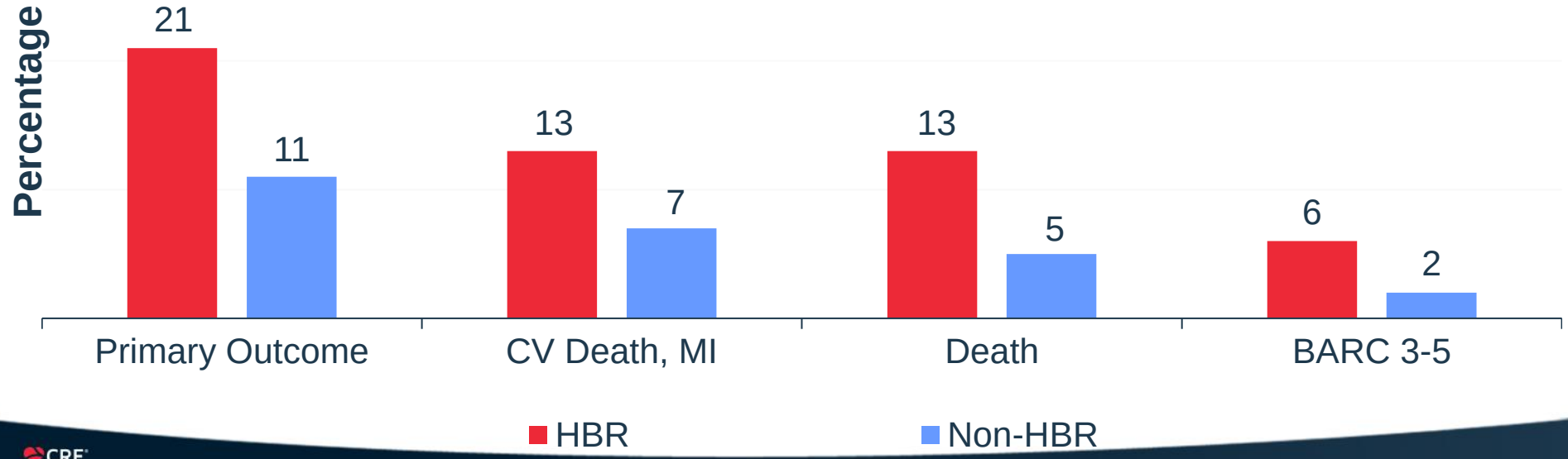
Study Endpoints

LESSON #1

HBR = HIGH ISCHEMIC RISK

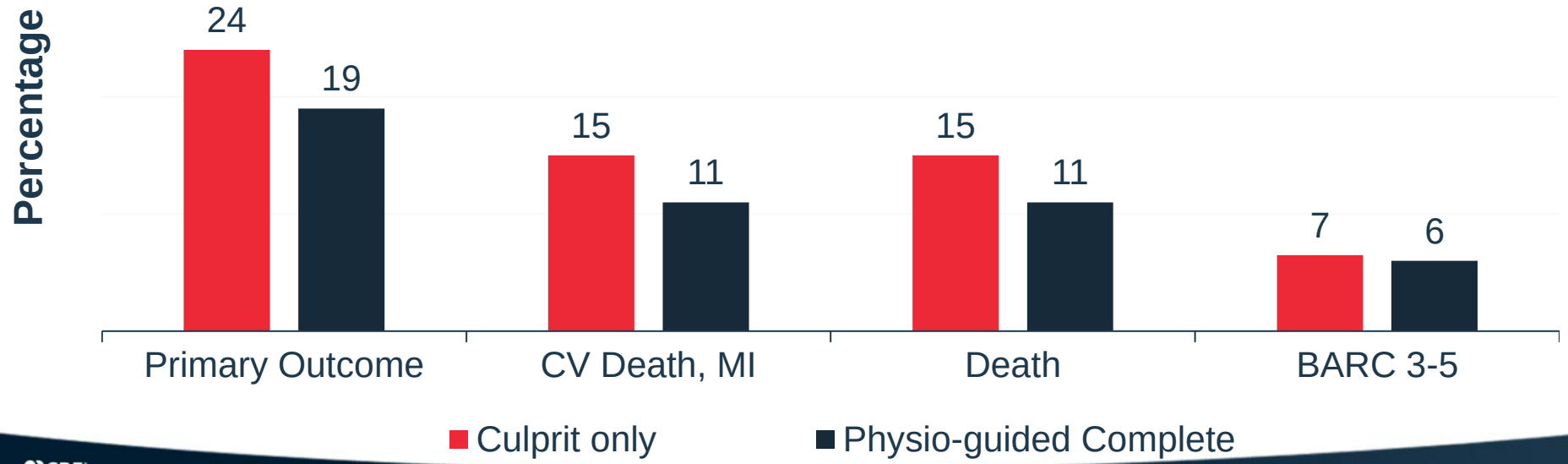


Study Endpoints

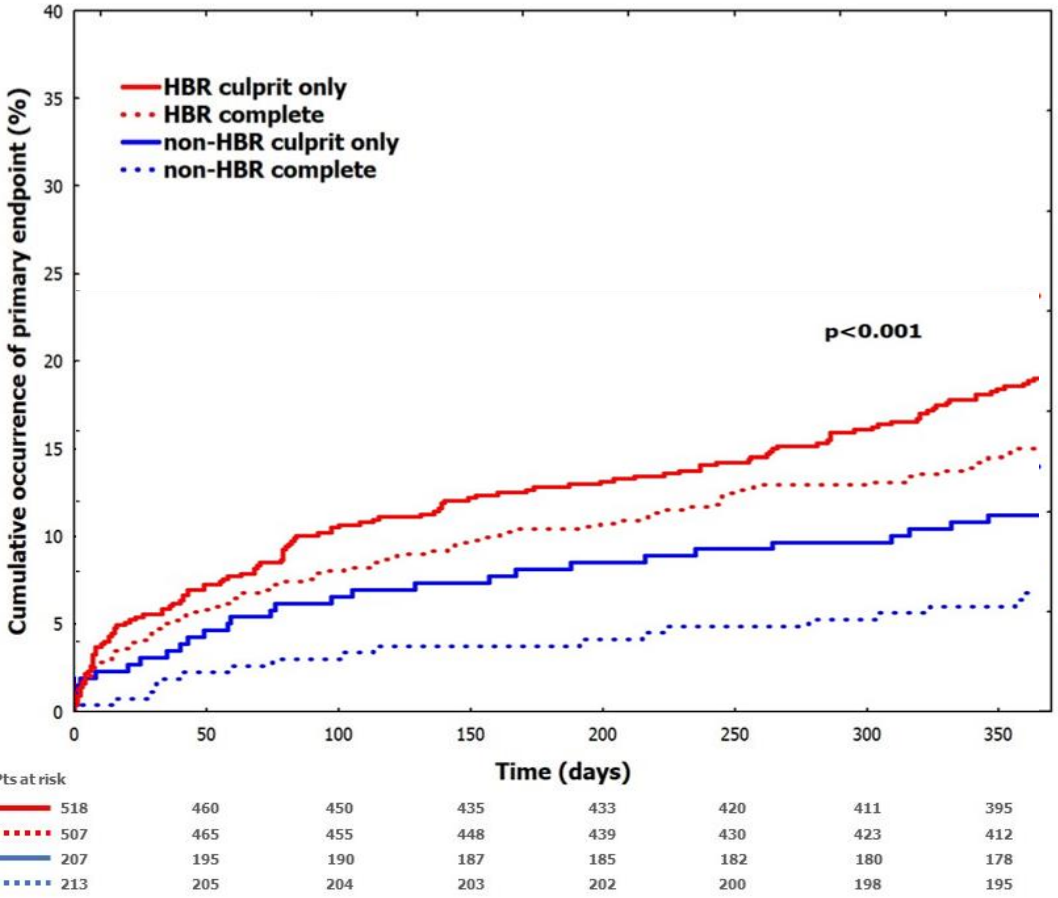
LESSON #2

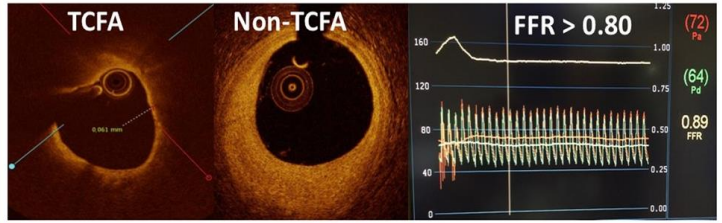
FFR/QFR ⬇ ISCHEMIC RISK in AMI

Primary Outcome	CV Death, MI	Death	BARC 3-5
p=0.043	*p=0.031*	*p=0.022*	*p=NS*

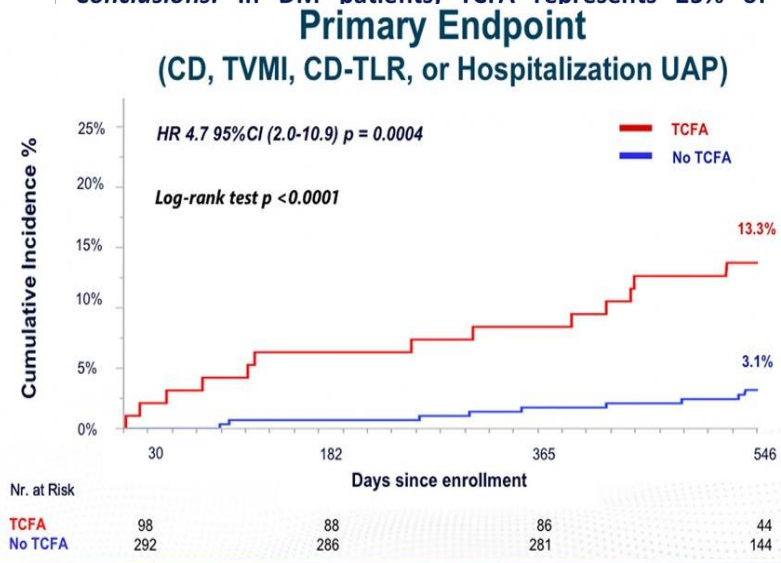


Primary Endpoint Met, but there is a VERY high residual risk





Conclusions: In DM patients, TCFA represents 25% of



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