

Functional versus Culprit-only Revascularization in Elderly Patients with Myocardial Infarction and Multivessel Disease



The FIRE trial

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on behalf of the FIRE trial Investigators

Background



- **Older patients (75+) are poorly represented in conventional randomized controlled trials**
- **The risk of periprocedural complications is higher and prognostically impactful older patients¹**
- **The benefit of complete revascularization in this subset of patients has been recently questioned²**

Research question



To investigate whether, in older patients (75+ years) with MI and multivessel disease, complete revascularization based on coronary physiology is superior to a culprit-only revascularization strategy

Study Organization

3 countries: Italy, Spain, Poland

34 centers

Study PI: Simone Biscaglia

Study Chair: Gianluca Campo

Executive Committee: Javier Escaned, Dariusz Dudek, Raul Moreno, Matteo Tebaldi, Emanuele Barbato

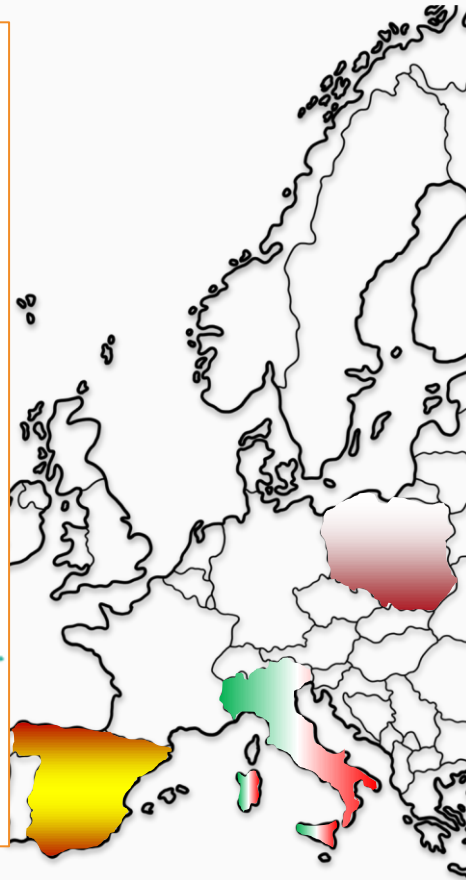


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CROs: AdvicePharma, Impulsae Consulting, KCRI



Sponsor:



Università degli Studi di Ferrara



Grant Suppliers:



Inclusion & Exclusion Criteria

Inclusion

- **75+ years old**
- **MI (STEMI or NSTEMI)**
- **Multivessel disease**
- **Successful PCI of culprit lesion**

Exclusion

- **Non culprit lesion on left main**
- **Unclear culprit lesion**
- **Life expectancy <1 year**
- **Prior CABG**
- **Planned surgical revasc**

Study 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

R

**Physiology-guided Complete
Revascularization**

Culprit-only Revascularization

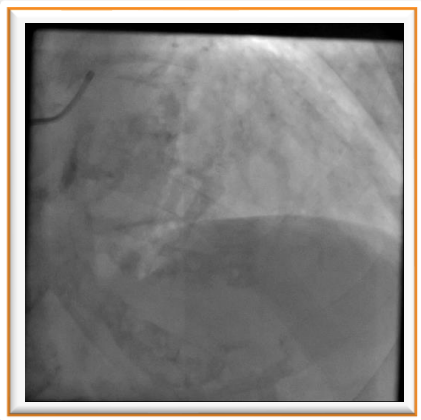
1-, 3-, and 5-year follow-up



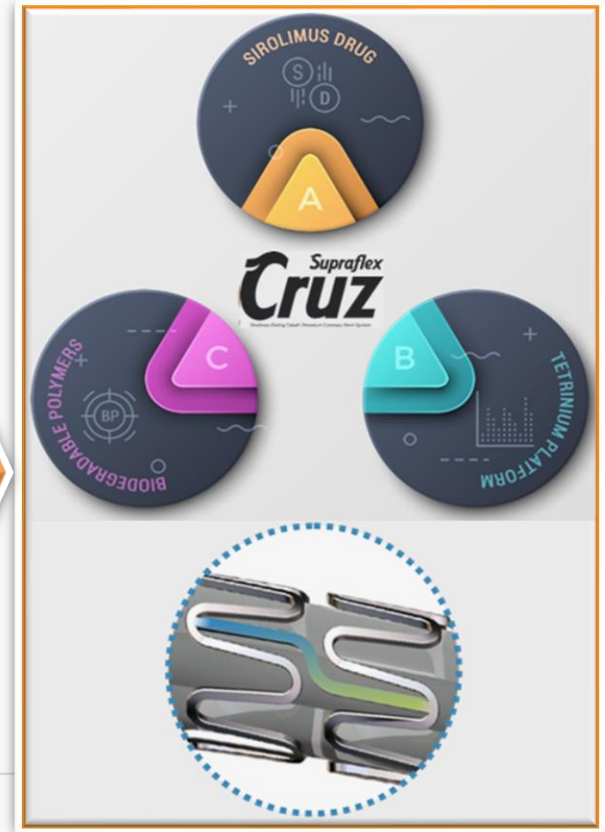
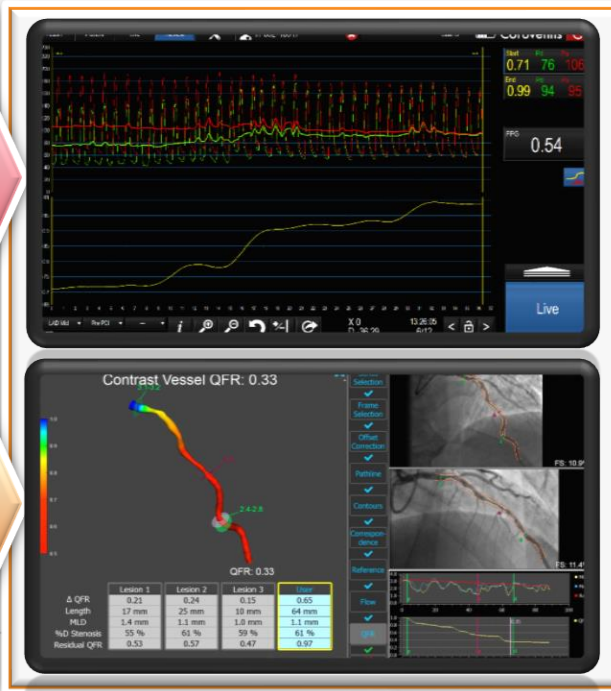
We estimated a conservative **15% rate** of the primary endpoint at 1 year in the culprit-only strategy group. Considering that functional assessment should **reduce the primary endpoint of at least 30%**, 1368 patients are required to have a 80% chance of detecting, as significant at the 5% level, a 30% difference in the primary outcome between the two groups

Coronary Physiology & Stents

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



OR



Study Endpoints



Primary endpoint

1-year death, any MI, any stroke, or id-revascularization

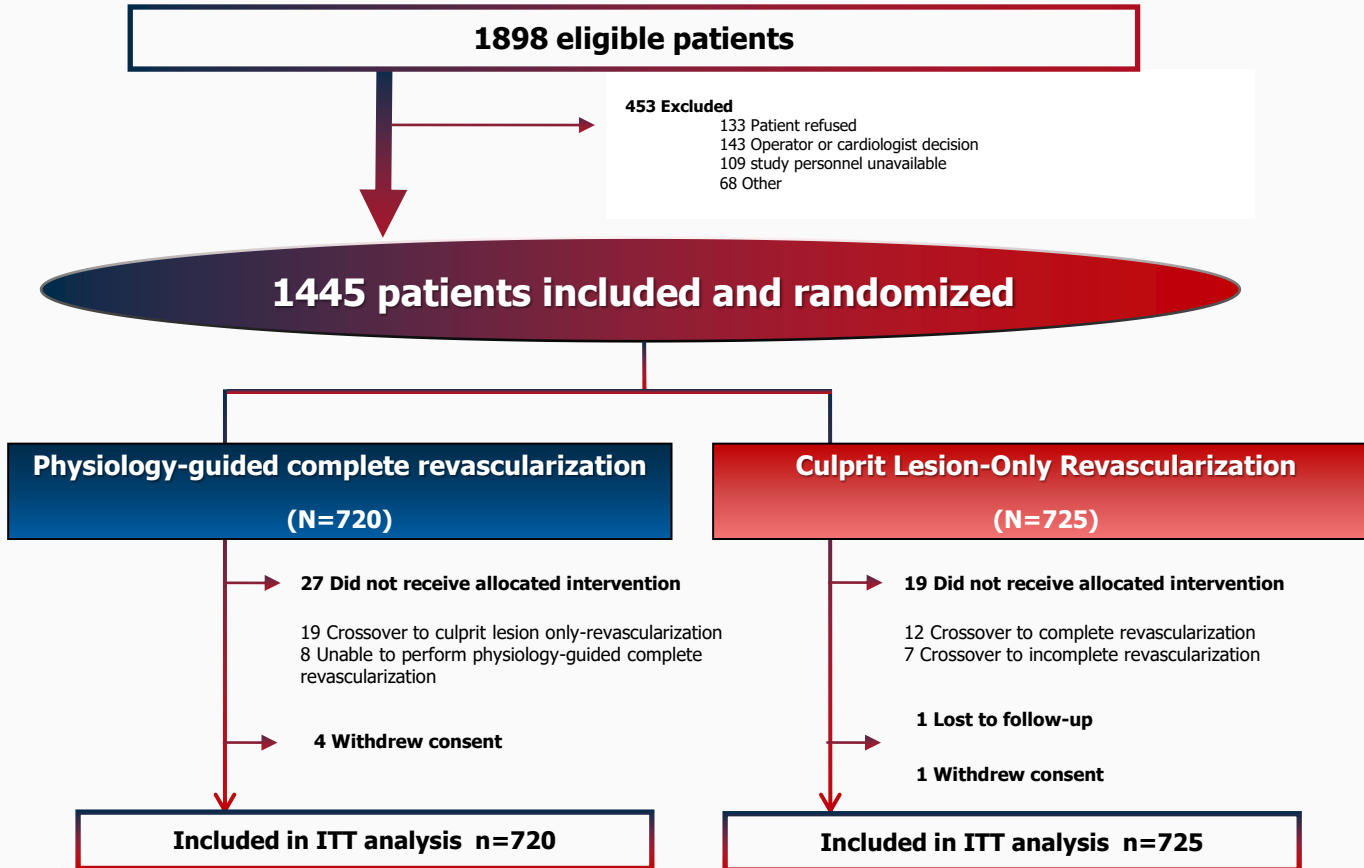
Key secondary endpoint

1-year cardiovascular death or MI

Safety endpoint

1-year CA-AKI, stroke, or BARC type 3-5 bleeding

Study flow-chart



- **76%** of eligible patients enrolled
- **2.6%** crossover from culprit-only
- Follow-up complete in **99.9%** of patients

Baseline Characteristics



Characteristic	Culprit-Only (N=725)	Physiology-Guided Complete (N=720)
Age (IQR) – yr	80 (77-84)	81 (77-84)
Female sex	265 (36.6)	263 (36.5)
Comorbidities		
Hypertension	592 (81.7)	593 (82.4)
Diabetes	233 (32.1)	230 (31.9)
Prior MI	116 (16)	104 (14.4)
eGFR <60 ml/min	332 (45.8)	330 (45.8)
PAD	127 (17.5)	122 (16.9)
Clinical presentation		
STEMI	256 (35.3)	253 (35.1)
NSTEMI	469 (64.7)	467 (64.9)

Characteristic	Culprit-Only (N=725)	Physiology-Guided Complete (N=720)
Killip class ≥ 2	208 (28.7)	204 (28.3)
Hospital LOS	5 (3-7)	6 (4-8)
Medication at discharge		
Aspirin	683 (94.2)	692 (96.1)
Clopidogrel	358 (49.4)	371 (51.5)
Ticagrelor	337 (46.5)	326 (45.3)
Prasugrel	16 (2.2)	16 (2.2)
Vitamin K antagonist	36 (5)	27 (3.8)
NOAC	129 (17.8)	137 (19)
ACEi or ARB	552 (76.1)	556 (77.2)
Statin	661 (91.2)	680 (94.4)

Procedural Characteristics



Characteristic	Culprit-Only (n=725)	Physiology-Guided Complete (N=720)
Procedures		
Total number	725	961
Days from index to staged procedures	-	3 (2-4)
Radial access	672 (92.7)	911 (94.8)
Number of non-culprit vessels per patient		
One	510 (70.3)	503 (69.9)
Two or more	215 (29.7)	217 (30.1)
Location of non-culprit vessels		
LAD	291 (30.6)	296 (31.2)
Circumflex artery	319 (33.5)	308 (32.5)
Right coronary artery	320 (33.6)	310 (32.7)
Ramus intermedius artery	21 (2.2)	34 (3.6)

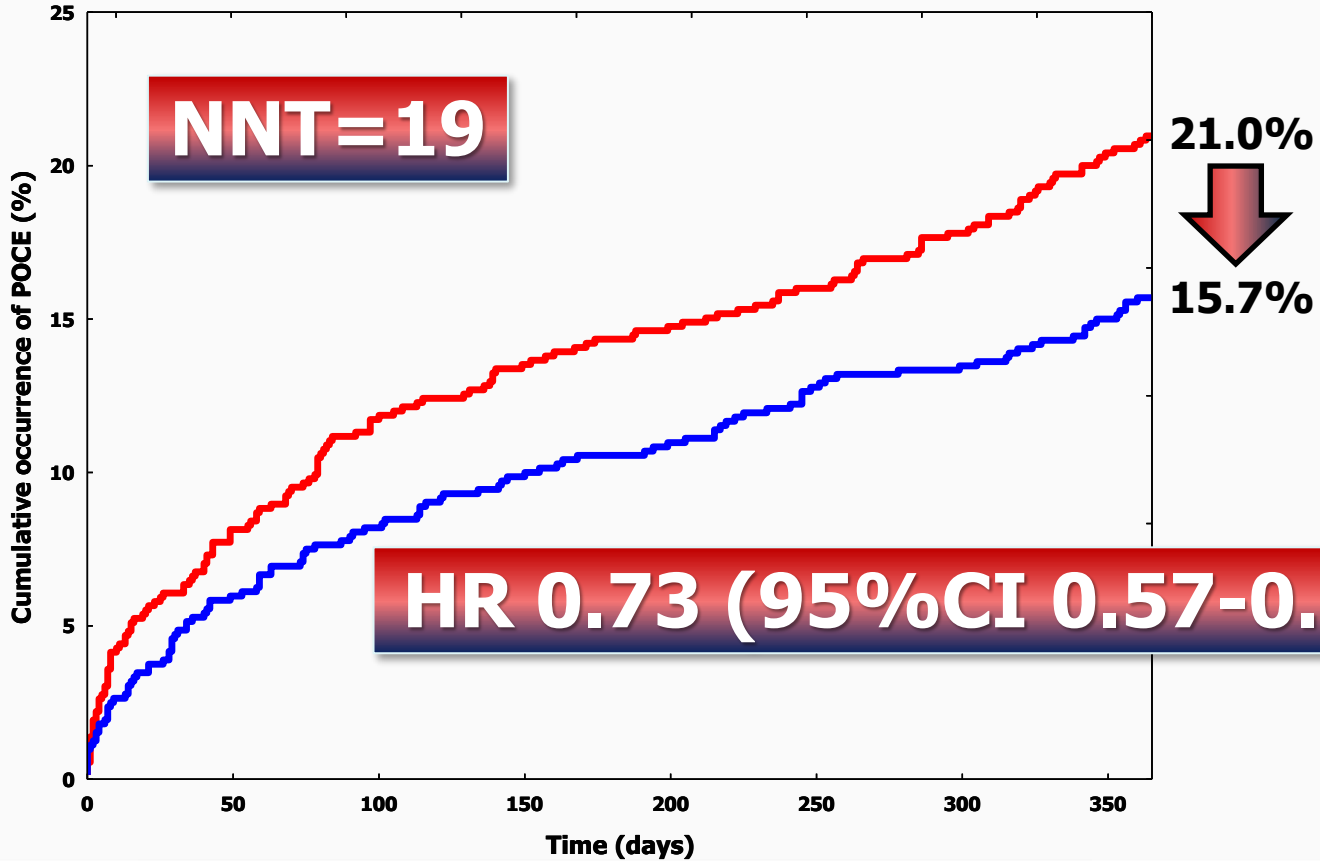
Characteristic	Culprit-Only (n=725)	Physiology-Guided Complete (N=720)
RVD	3.0 (2.5-3.0)	3.0 (2.5-3.0)
Diameter stenosis	70 (60-80)	70 (60-80)
Percent diameter stenosis		
50-69%	401 (42.2)	390 (41.1)
70-89%	378 (39.7)	380 (40.1)
90-99%	172 (18.1)	178 (18.8)
Type of physiological assessment		
Wire-based hyperemic	-	451 (49.6)
Wire-based non hyperemic	-	138 (15.2)
Angiography-based index	-	320 (35.2)
Functionally significant non-culprit vessel	-	425 (44.8)

Primary endpoint

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



- Culprit-only
- Physio-guided Complete

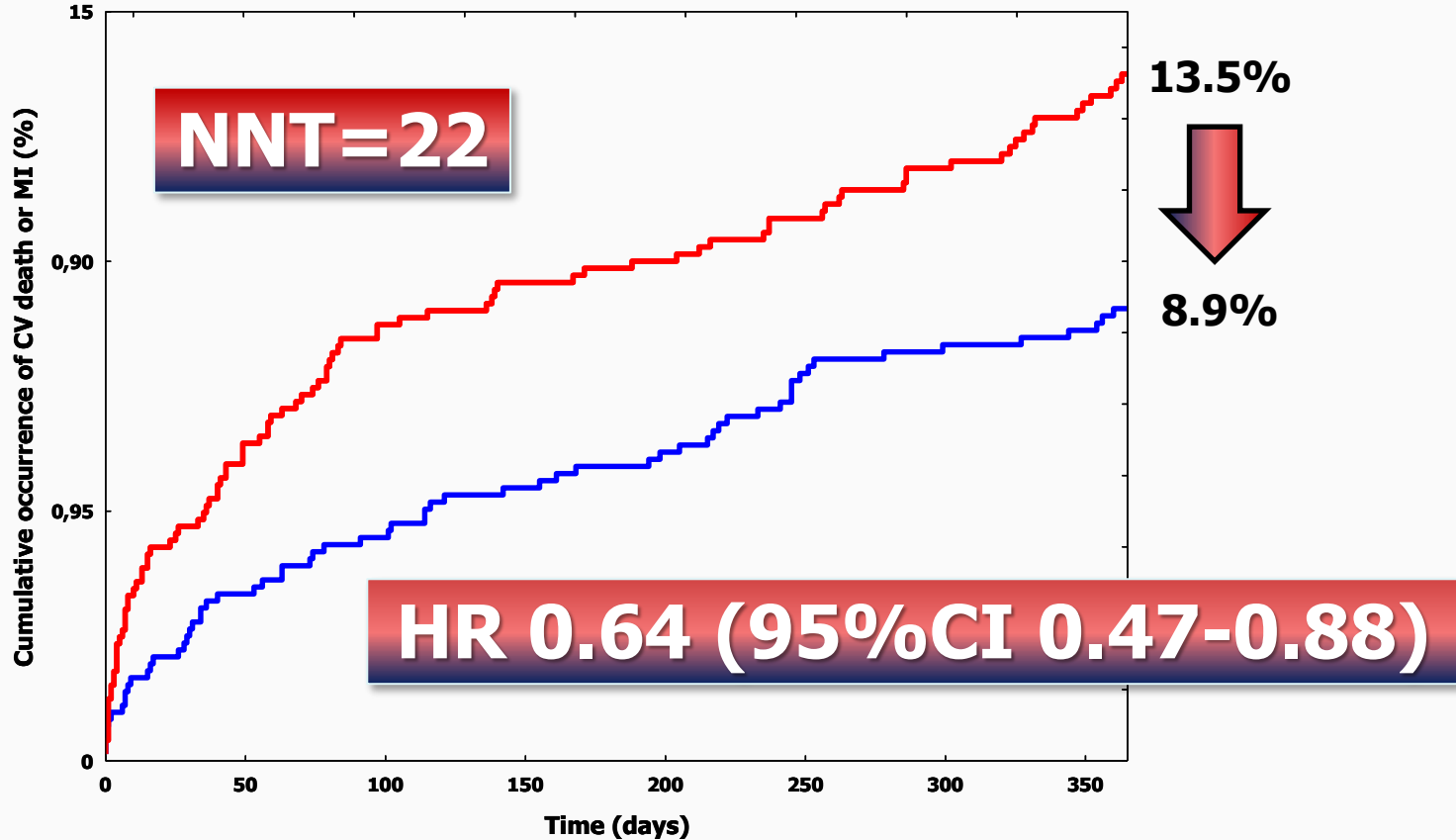


Key secondary endpoint

CV death or MI



- Culprit-only
- Physio-guided Complete



Safety and Secondary Endpoints



Outcome	Culprit-Only	Complete	Hazard Risk (95% CI)
	(n=725) no. (%)	(n=720) no. (%)	
Death	93 (12.8)	66 (9.2)	0.70 (0.51-0.96)
Cardiovascular death	56 (7.7)	36 (5)	0.64 (0.42-0.97)
Non-cardiovascular death	37 (5.1)	30 (4.2)	0.82 (0.50-1.32)
Stroke	7 (1.0)	12 (1.7)	1.73 (0.68-4.40)
Myocardial infarction	51 (7.0)	32 (4.4)	0.62 (0.40-0.97)
Ischemia-driven revascularization	49 (6.8)	31 (4.3)	0.63 (0.40-0.98)
Safety endpoint*	148 (20.4)	162 (22.5)	1.11 (0.89-1.37)

Study limitations



- **Open label study**
- **Our results may not apply to:**
 - **Complete revascularization outside index hospitalization**
 - **Complete revascularization guided by conventional angiography**
 - **Patients not treated with biodegradable-polymer sirolimus eluting stent**



Conclusions

Among patients aged 75 years or older with MI and multivessel disease, physiology-guided complete revascularization, as compared to a culprit-only revascularization strategy, reduced

- **Composite of death, MI, stroke, or ischemia-driven revasc**
- **Cardiovascular death or MI**



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