What Have We Learned from 35 Years of TIMI Trials?

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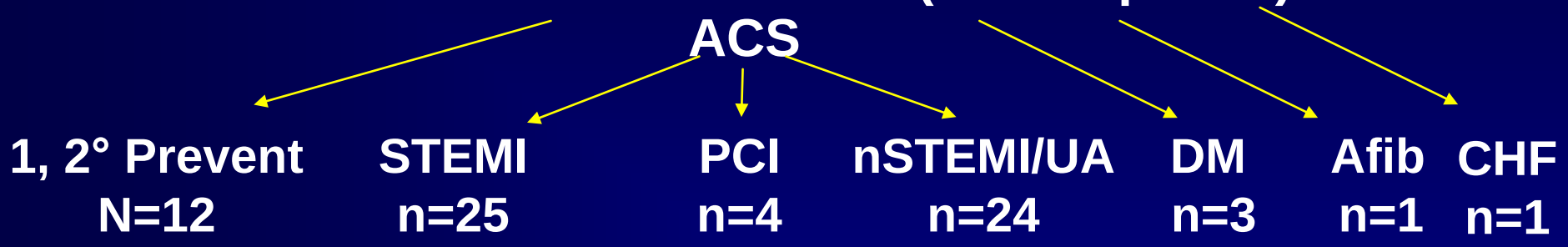
TIMI Trials
1984-2019

70 Cardiovascular Trials (68 completed)



- 300,000 Patients enrolled to date
- 4000 Hospitals worldwide
- 8000 Investigators worldwide
- 52 Countries
- 6 Continents

TIMI BIBLIOGRAPHY: >1000 PEER REVIEWED PUBLICATIONS

Top 10 Lessons 1984-1999

1. Better epicardial flow results in lower mortality
2. Development of grading scale for bleeding
3. Speed of flow (frame count) and perfusion of myocardial tissue (perfusion grade) are impt
4. tPA is better than SK at opening arteries
5. Single bolus TNK-tPA is safe and effective
6. Enoxaparin is superior to unfractionated heparin
7. Risk score predicts outcomes, can guide therapy
8. Early invasive approach is better in UA/nSTE-MI
9. Prehospital lytic is feasible and speeds reperfusion
10. Multimarker approach improves prognostic ability

The Prior Decade (2000-2009)

1. Established the risk/benefit for clopidogrel (CLARITY-TIMI 28) and enoxaparin (ExTRACT-TIMI 25) as adjuncts to fibrinolysis for STEMI
2. Intensive statin is better than moderate statin post ACS (PROVE IT-TIMI 22)
3. Prasugrel in ACS treated with PCI (TRITON-TIMI 38)
4. Early Routine vs Late Provisional Use of Eptifibatide (IV GP IIb/IIIa) in nSTE-ACS (EARLY-ACS)
5. Ranolazine in nSTE-ACS (MERLIN-TIMI 36)

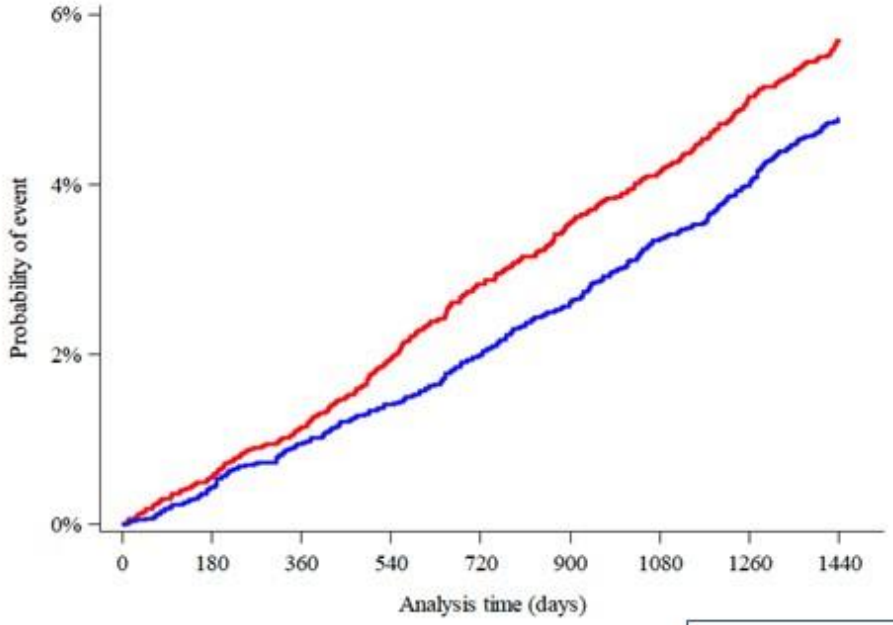
TIMI Trials 2010-present

Population	Experimental Therapy
ACS	antiplatelet, anti-inflammatory
Post ACS	oral factor Xa, Lp-PLA_2 inhibitor
Lipid-lowering	ezetimibe, PCSK9, CETP
Diabetes	inhibitors of DPP-4, SGLT-2
Atrial Fib	oral factor Xa
Metabolic syndr.	serotonin receptor agonist
Heart failure	neprilysin inhibitor

Primary Endpoints

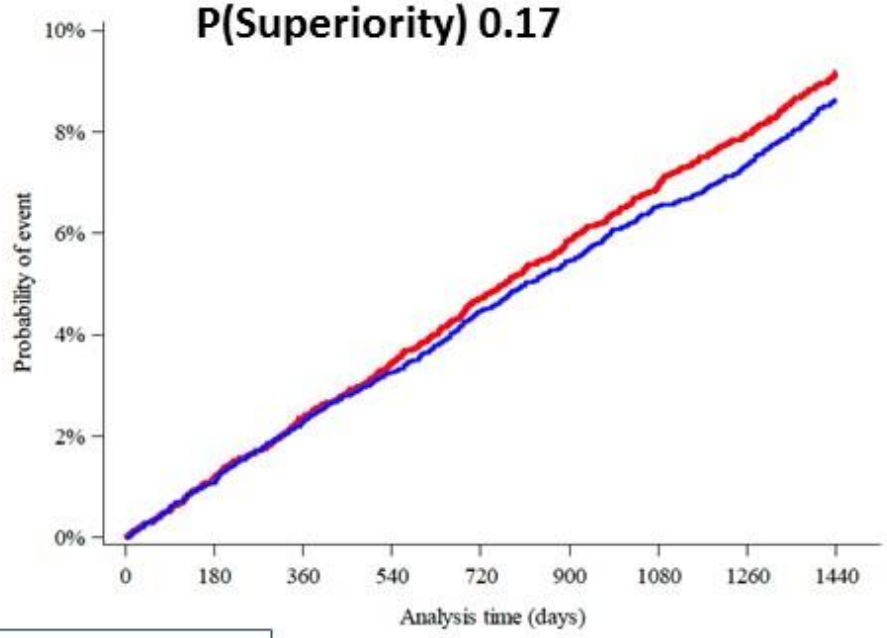
CVD/HHF

4.9% vs 5.8%
HR 0.83 (0.73-0.95)
P(Superiority) 0.005



MACE

8.8% vs 9.4%
HR 0.93 (0.84-1.03)
P(Noninferiority) <0.001
P(Superiority) 0.17



Dapagliflozin
Placebo

Wiviott SD, N Engl J Med 2019; 380:347-357

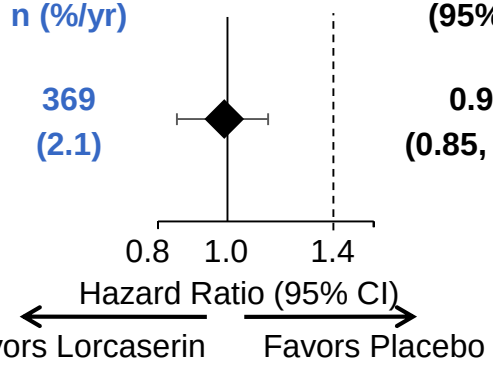
Primary CV Outcomes

Camellia
Cardiovascular And Metabolic Effects of Lorcaserin In Overweight And Obese Patients
TIMI 61

N = 12,000

CV Death, MI, Stroke (Safety)

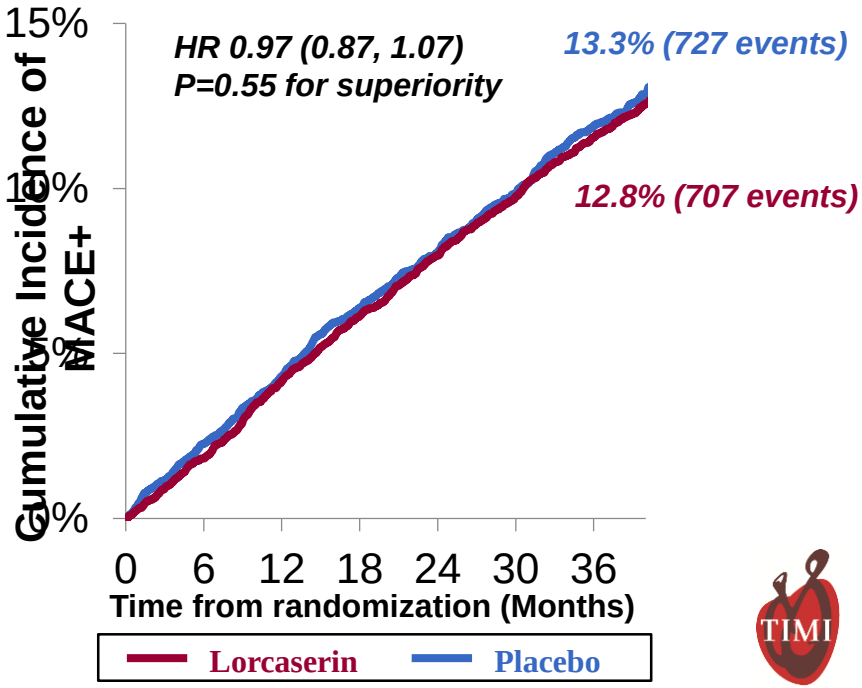
	Lorc n (%/yr)	Pbo n (%/yr)	MACE HR (95%CI)
CV death, MI, or stroke	364 (2.0)	369 (2.1)	0.99* (0.85, 1.14)



P (non-inferiority) < 0.001

****Non-inferiority boundary: HR 97.5% upper bound of 1.4***

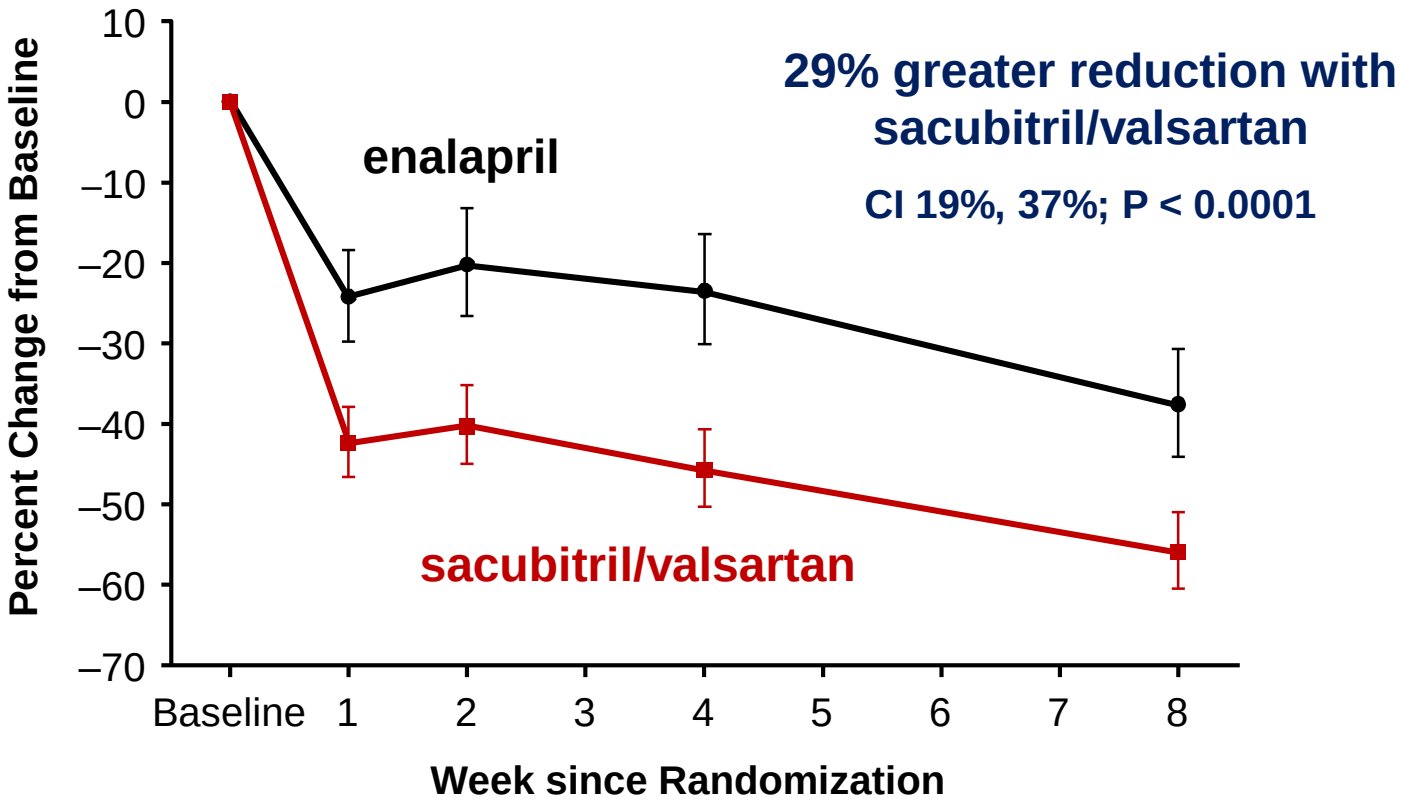
CV Death, MI, Stroke, HF, Hosp for UA, Cor Revasc (Efficacy)



TIMI

Bohula EA et al. New Engl J Med 2018

Primary Endpoint: % Change in NT-proBNP



Velazquez EJ, NEJM 2018 (online DOI: 10.1056/NEJMoa1812851

Goals of Clinical Trials

- Identify new treatments
- Bring new drugs/devices into the clinic
- Extend indications on existing therapies
- Test new strategies
- Provide new insights
- Change guidelines for care

Improve outcomes for our patients