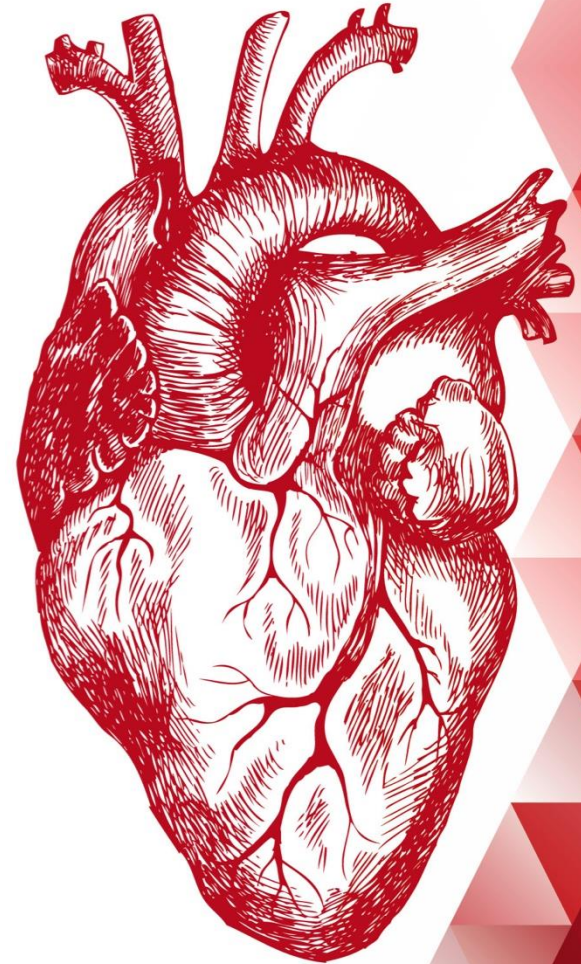


# STREAM TRIAL

WHY A PHARMACO-INVASIVE  
APPROACH IS ESSENTIAL



# STREAM

# TRIAL



**ST**RATEGIC **R**EPERFUSION **E**ARLY **A**FTER **M**I

## **Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction**

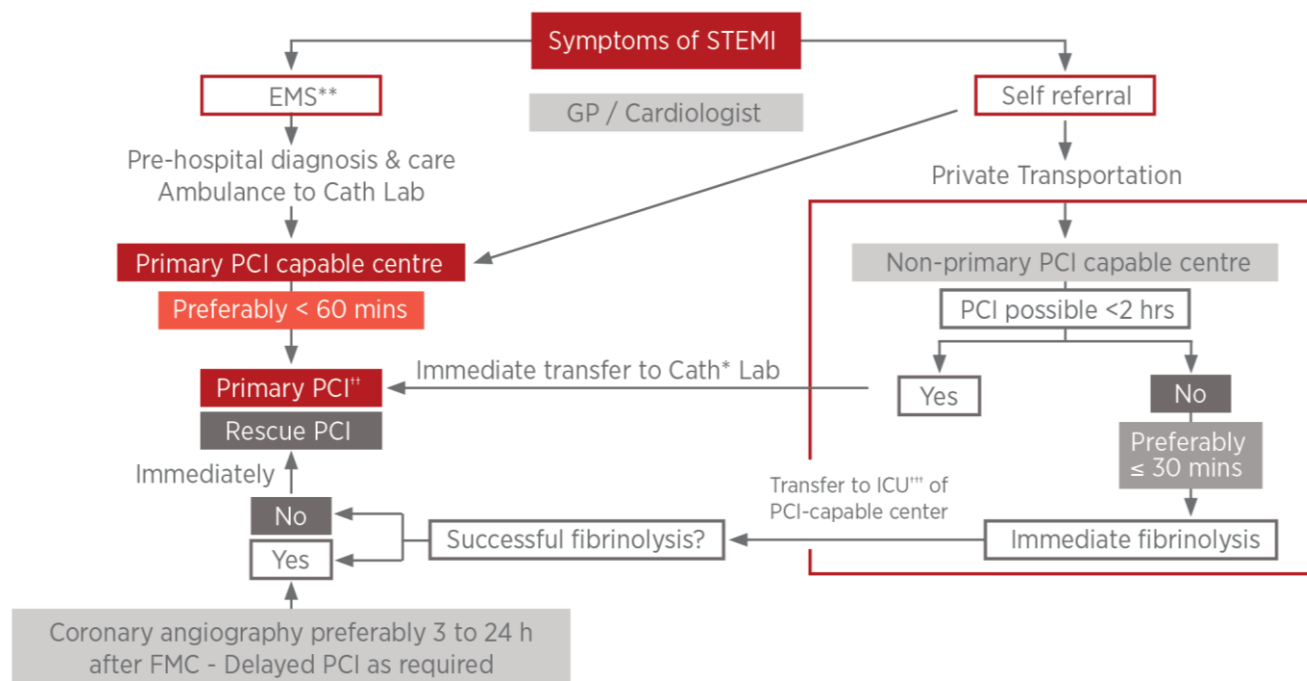
PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# ESC GUIDELINES ON ACUTE STEMI MANAGEMENT

## ORGANISATION OF STEMI PATIENT DISPOSAL DESCRIBING PRE- AND IN-HOSPITAL MANAGEMENT, AND REPERFUSION STRATEGIES WITHIN 24H OF FMC<sup>†</sup>



\* Cath = Catheterisation Laboratory; \*\* EMS = Emergency Medical System; † FMC = First Medical Contact; †† PCI = Percutaneous Coronary Intervention; ††† ICU = Intensive Care Unit

Adapted from:  
Steg PG, James S. 2012 ESC Guidelines on acute myocardial infarction (STEMI). European Heart Journal. 2012;33:2501-2.

# STREAM (STRATEGIC REPERFUSION EARLY AFTER MYOCARDIAL INFARCTION)



Investigated whether prompt thrombolysis at first medical contact (FMC), followed by timely angiography or rescue PCI in patients with acute STEMI presenting within 3 hr not able to undergo PPCI within 60 min, is an appropriate and effective reperfusion treatment (pharmaco-invasive strategy) to PPCI



## **PRIMARY ENDPOINT:**

composite of death, shock, congestive heart failure (CHF) or re-infarction at 30 days

**SAFETY ENDPOINTS INCLUDE:** all-cause mortality, cardiogenic shock, CHF, re-infarction, rehospitalisation for cardiac reasons and rehospitalisation for non-cardiac reasons

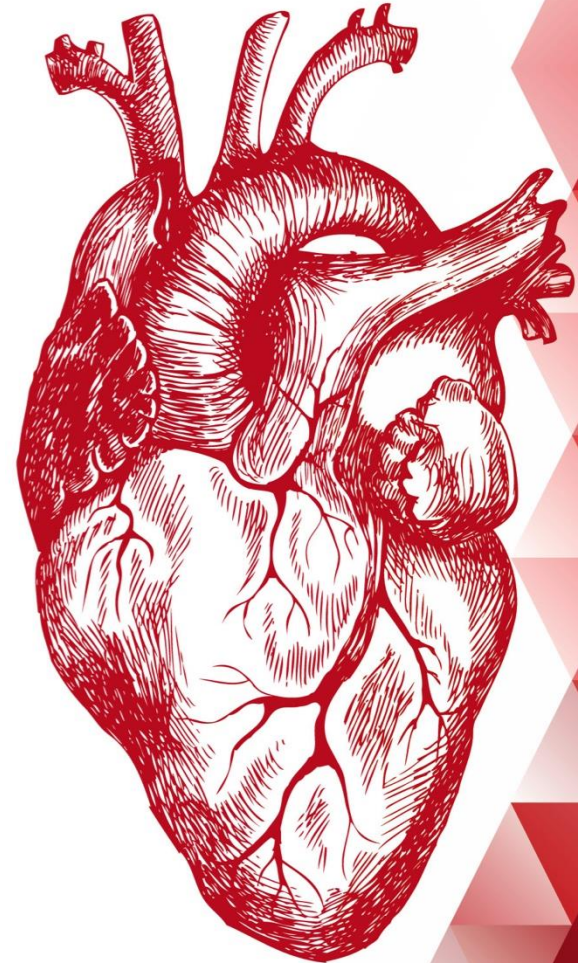
FMC = First Medical Contact; PCI = Percutaneous Coronary Intervention; PPCI = Primary Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# STREAM TRIAL AIM

To compare the outcome of early fibrinolysis with Tenecteplase followed by coronary angiography within 6-24 hours with standard primary PCI in STEMI patients presenting within 3 hours of symptom onset and unable to undergo primary PCI within 1 hour.



PCI = Percutaneous Coronary Intervention



## AIM OF STUDY



**Are there other therapies we can use in STEMI patients who cannot receive a primary PCI < 1 hr?**

**Therefore the STREAM investigators asked:**

How does early thrombolysis with anti-platelet and anticoagulant therapy compare to primary PCI in STEMI patients who present <3 hours of symptom onset?

PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# COMPARING OUTCOMES OF FIBRINOLYSIS VERSUS PPCI

## *The* NEW ENGLAND JOURNAL *of* MEDICINE

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### Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction

Paul W. Armstrong, M.D., Anthony H. Gershlick, M.D., Patrick Goldstein, M.D., Robert Wilcox, M.D.,  
Thierry Danays, M.D., Yves Lambert, M.D., Vitaly Sulimov, M.D., Ph.D., Fernando Rosell Ortiz, M.D., Ph.D.,  
Miodrag Ostojic, M.D., Ph.D., Robert C. Welsh, M.D., Antonio C. Carvalho, M.D., Ph.D., John Nanas, M.D., Ph.D.,  
Hans-Richard Arntz, M.D., Ph.D., Sigrun Halvorsen, M.D., Ph.D., Kurt Huber, M.D., Stefan Grajek, M.D., Ph.D.,  
Claudio Fresco, M.D., Erich Bluhmki, M.D., Ph.D., Anne Regelin, Ph.D., Katleen Vandenberghe, Ph.D.,  
Kris Bogaerts, Ph.D., and Frans Van de Werf, M.D., Ph.D., for the STREAM Investigative Team\*

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# STREAM TRIAL STUDY ARMS

## ARM 1:

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Tenecteplase (Metalyse® ) followed by angiography after 6-24 hours unless rescue is needed

## ARM 2:

---

Primary PCI according to local standards

PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.





## END POINTS



### **PRIMARY END POINT (30 DAY COMPOSITE):**

---

Death from any cause, shock, congestive HF, or re-infarction

### **SINGLE EFFICACY OR SAFETY END POINTS INCLUDED:**

---

- Ischaemic stroke
- ICH
- Non-intracranial bleeding

HF = Heart Failure

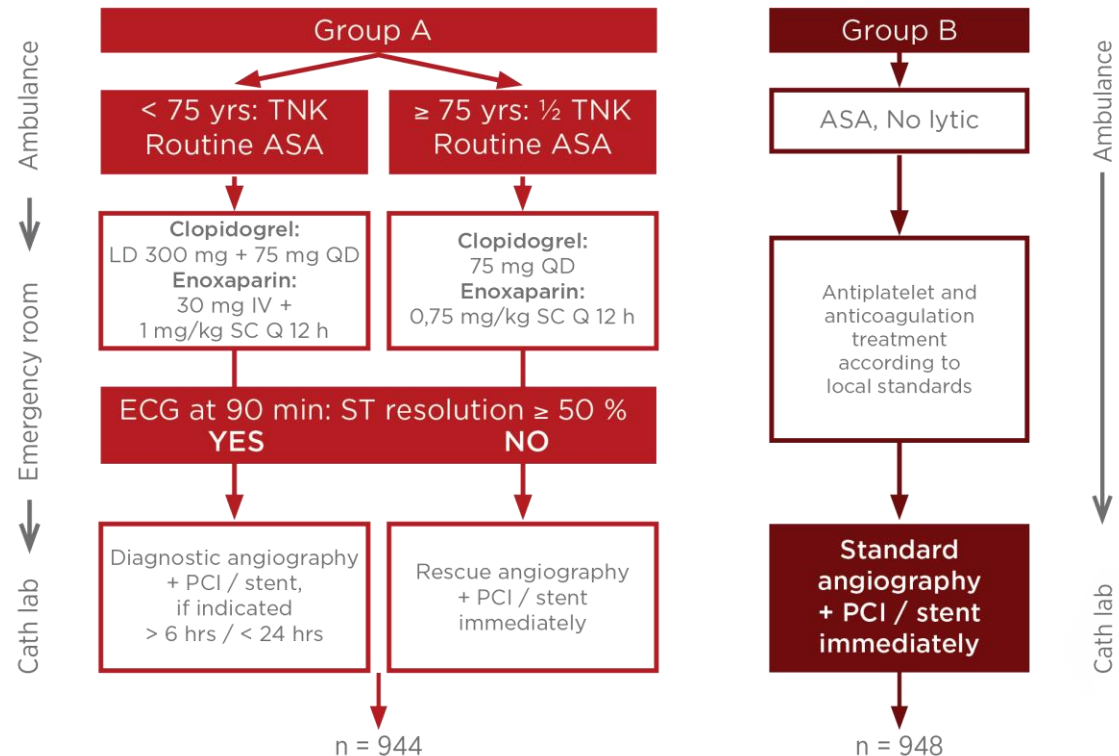
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Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# STREAM STUDY DESIGN

**PATIENTS PRESENTING WITH STEMI <3HRS FROM ONSET OF SYMPTOMS THAT CANNOT RELIABLY UNDERGO PRIMARY PCI <60 MIN**



Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.

# RESULTS



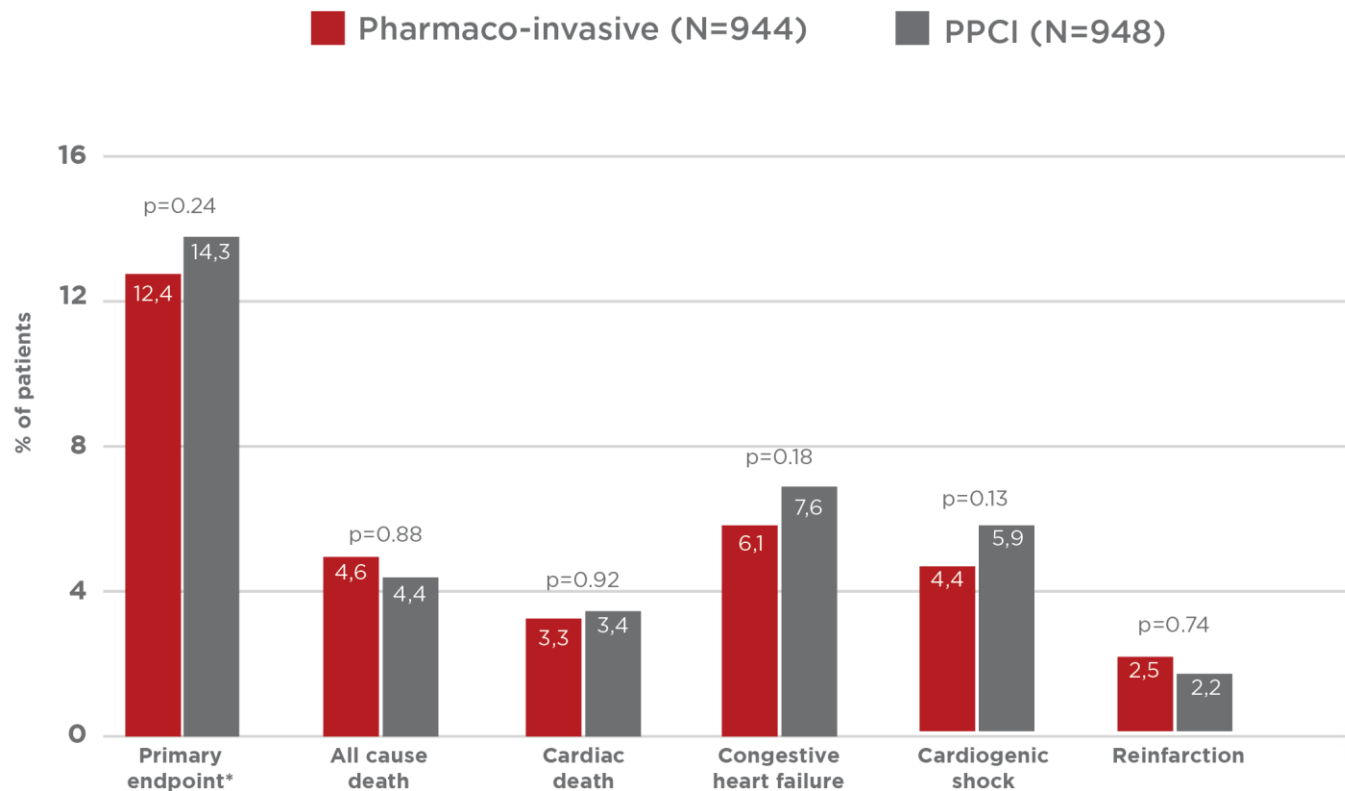
	Fibronolysis	Primary PCI	P value
Primary end point	12.4%	14.3%	0.21
Symptom onset to start of reperfusion treatment: tenecteplase or arterial sheath insertion (min)	<b>100</b>	178	<0.0001
Open vessels on first angiography (before PCI)	58.5%	20.7%	<0.0001
PCI after angiography	80.4%	89.8%	<0.0001
CABG after angiography/PCI	4.7%	2.1%	0.002
Stent placement	95.7%	95.6%	0.95

- No difference in primary end point i.e. mortality and morbidity
- Shorter delay for patients receiving treatment in fibronolysis
- Better initial revascularization in patients receiving fibronolysis
- Less patients required a PCI after thrombolysis in arm 1 vs arm 2
- Increased number of patients needed CABG in the fibronolysis — due to longer time to angiography where revascularization decisions would be made

PCI = Percutaneous Coronary Intervention;

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.

# STREAM: INCIDENCE & INDIVIDUAL COMPONENTS OF THE PRIMARY ENDPOINT AT 30 DAYS



\* death from any cause, shock, congestive heart failure, or reinfarction up to 30 days  
PPCI: Primary Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



## STROKE INCIDENCE

	<b>Fibronolysis (N = 944)</b>	<b>Primary PCI (N = 948)</b>	<b>P value</b>
Event	no./total no. (%)		
Total stroke	15/939 (1.6)	5/946 (0.5)	0.03
Intracranial hemorrhage			
Any	9/939 (1.0)	2/946 (0.2)	0.04
After protocol amendment*	4/747 (0.5)	2/756 (0.3)	0.45

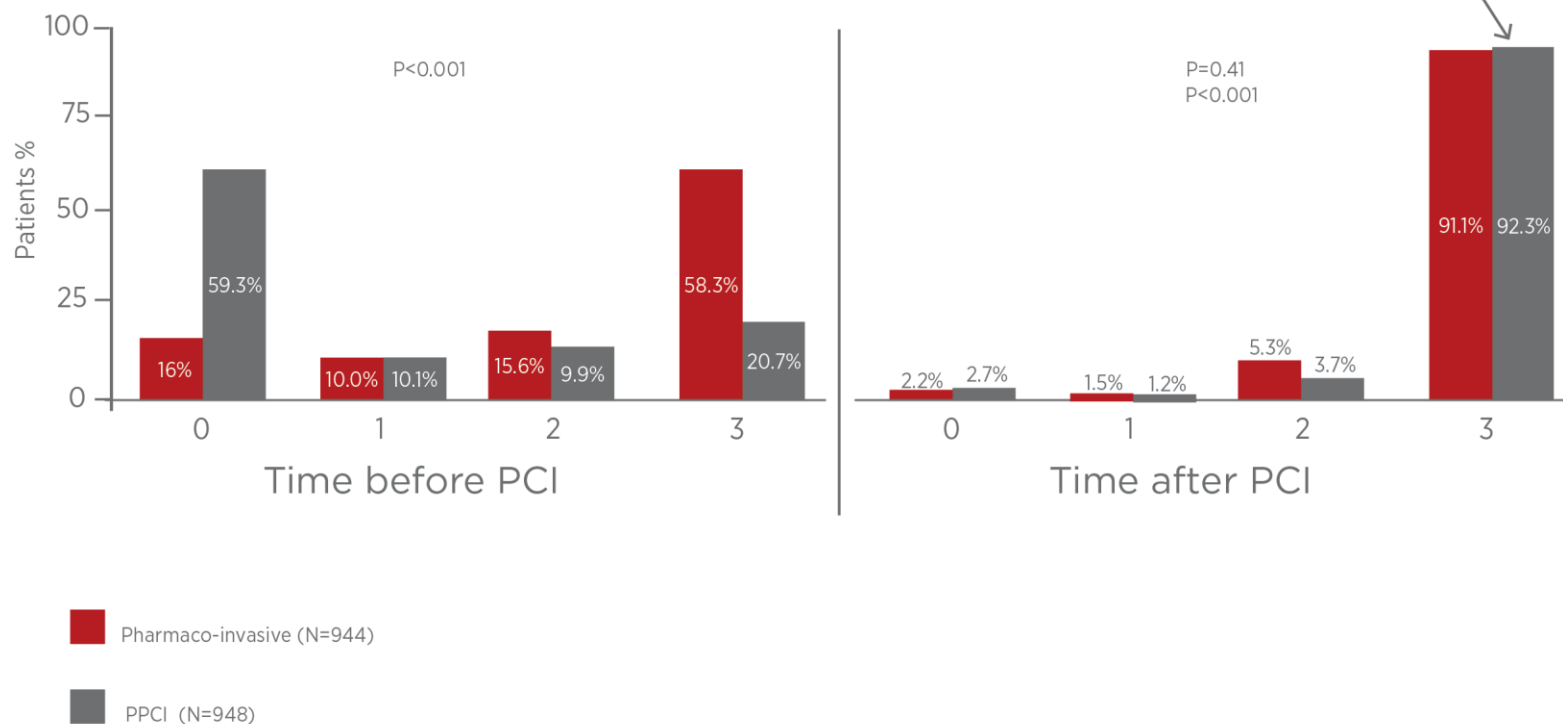
**After amendment: No difference in incidence of intracranial haemorrhage between 2 treatment groups**

PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# TIMI FLOW RATES



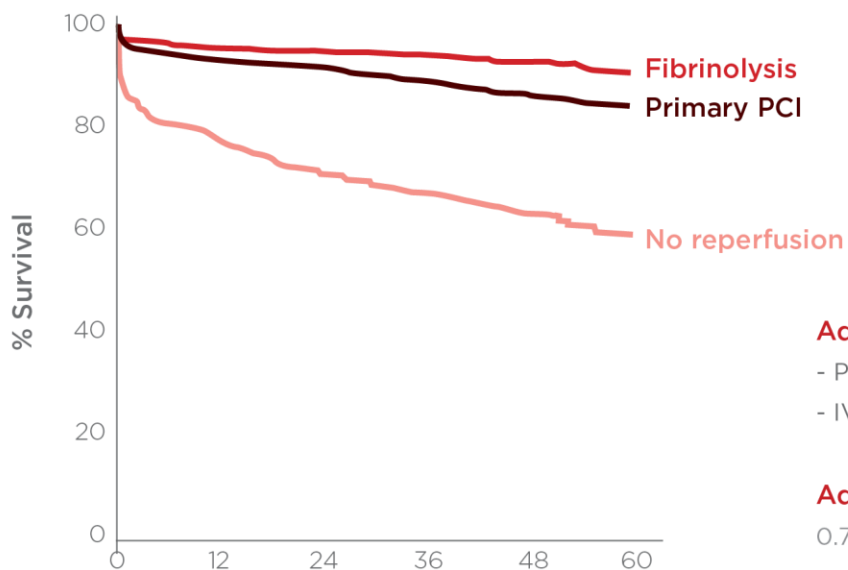
PPCI = primary percutaneous coronary intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.





# FAST-AML COHORT CONFIRMS OUTCOMES LONG TERM



## Adjusted HR [95% CI] (reference no reperfusion)

- Primary PCI: 0.57 [0.43 - 0.74]
- IV Fibrinolysis: 0.48 [0.35 - 0.68]

## Adjusted HR [95% CI] fibrinolysis vs pPCI

0.73 [0.50 - 1.06]

### Numbers at risk

	Months			
No reperfusion	462	314	277	248
Lysis	447	413	395	362
PPCI	583	524	476	439

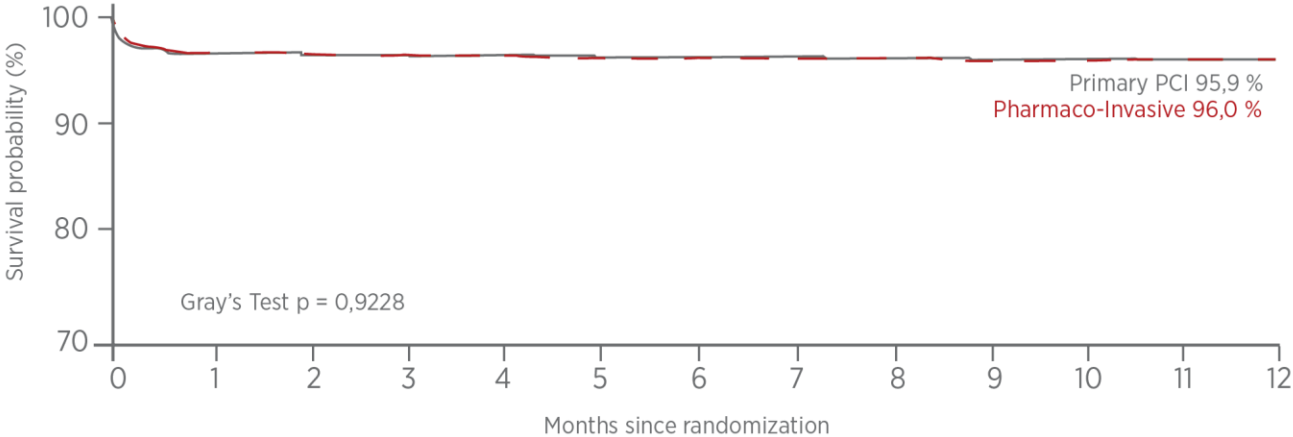
PPCI = primary percutaneous coronary intervention

Adapted from:  
Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



# STREAM RESULTS: MORTALITY

Cardiac mortality cumulative incidence STREAM trial



Number at Risk													
Tenecteplase	944	896	888	886	884	881	880	879	878	875	875	874	873
Primary PCI	948	903	898	897	893	890	890	889	888	887	886	885	885

PCI = Percutaneous Coronary Intervention

Sinnaeve PR, Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Lambert Y, Danays T, Soulat L, Halvorsen S, Ortiz FR, Vandenberghe K. St-segment-elevation Myocardial Infarction Patients Randomized to a Pharmaco-invasive Strategy or Primary Percutaneous Coronary Intervention: Strategic Reperfusion Early After Myocardial Infarction (stream) 1-year Mortality Follow-up. Circulation. 2014 Sep 30;130(14):1139-45.



## STREAM STUDY CONCLUSIONS



### **FIBRINOLYSIS WITH BOLUS TENECTEPLASE AND CONTEMPORARY ANTITHROMBOTIC THERAPY GIVEN BEFORE TRANSPORT TO A PCL-CAPABLE HOSPITAL:**

- 
- Circumvents the need for urgent PCI in about two thirds of fibrinolytic treated STEMI patients
  - Is associated with small increased risk of intracranial bleeding
  - Is as effective as PPCI in STEMI patients within 3 hours symptom onset who cannot undergo PCI within 1 hour of first medical contact



## SUBGROUP ANALYSIS



**No difference in treatment effect of fibrinolysis vs. primary PCI in patients regardless of:**

---

- Age
- Gender
- Blood Pressure
- Presence of diabetes mellitus
- Weight

The results are similar in different population groups

PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



## IMPORTANT TAKE HOME POINTS

- Fibrinolysis provides clinicians with additional time **BUT 80% of patients will still require a PCI**
- A **greater incidence of ICH** was seen in patients before the protocol was amended, after which there was **no significant difference** between groups
- Blood pressure, age, gender, diabetes etc **does not influence impact of fibrinolysis** on primary outcome

PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.



## WHAT DOES THIS MEAN?



- Clinicians can “buy time” by administering tenecteplase to STEM I patients if primary PCI cannot be performed within 1 hour

- 
- Of importance in SA setting:
    - Traffic, patients living in outlying areas
    - Not all hospitals have PCI facilities

- 
- Provide additional time for patient to receive PCI with similar outcomes

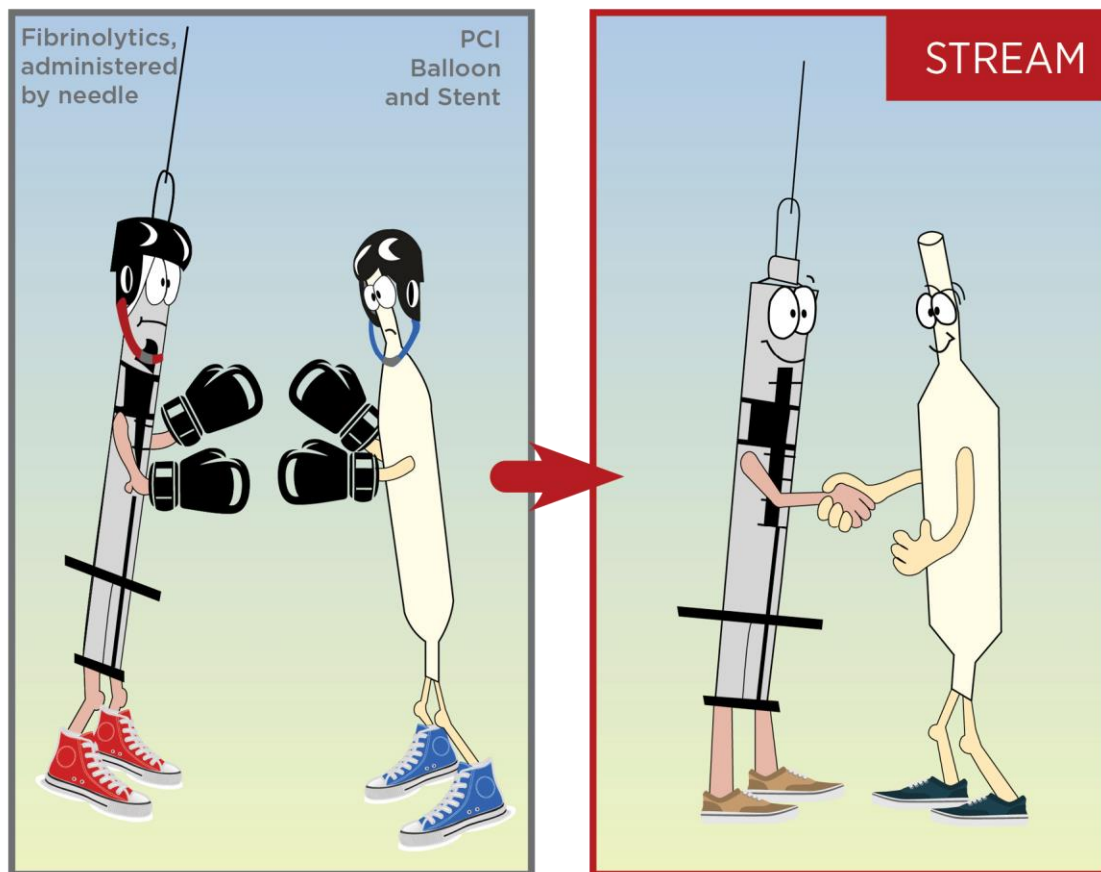
PCI = Percutaneous Coronary Intervention

REFERENCE HERE





# STREAM: NEW APPROACH IN ACUTE STEMI MANAGEMENT



PCI = Percutaneous Coronary Intervention

Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.

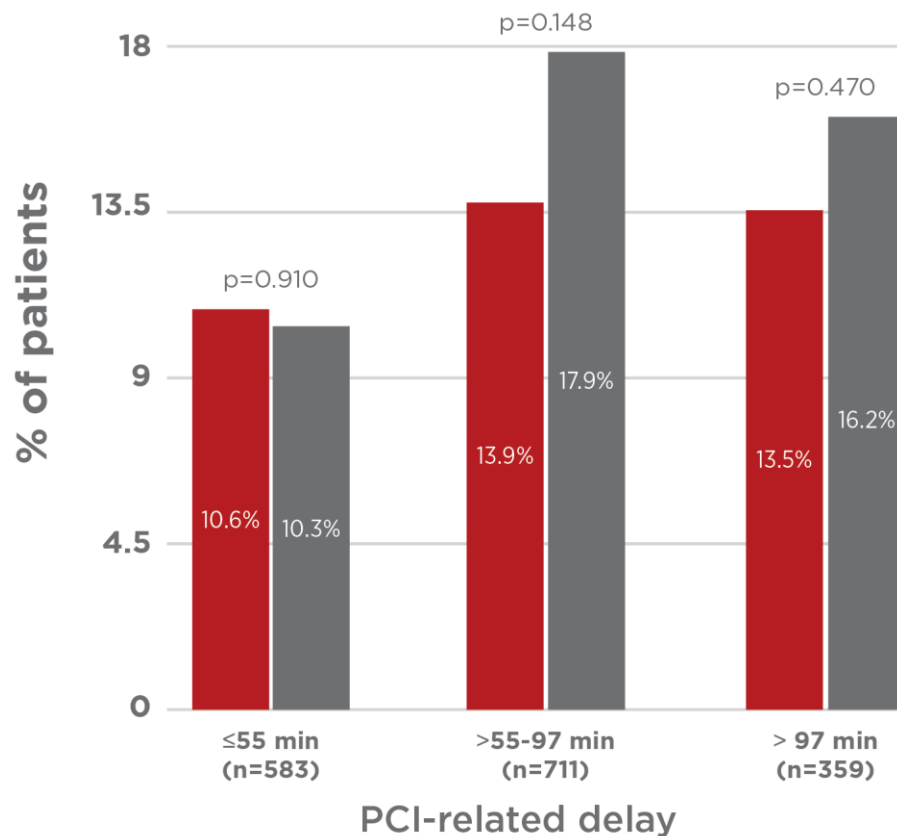
# STREAM: UPDATES

1. STREAM Time Delay
2. STREAM Aborted MI
3. ECG Insights into Strategic Reperfusion
4. STREAM Elderly Patients
5. STREAM 1-Year Mortality Follow-Up
6. STREAM Cardiac Results





## STREAM: TIME DELAY



- Assessed the impact of increasing time delay on outcomes in patients randomised to pharmaco-invasive strategy or PPCI
- Composite\* endpoint according to time delay:

■ Pharmaco-invasive  
■ PPCI

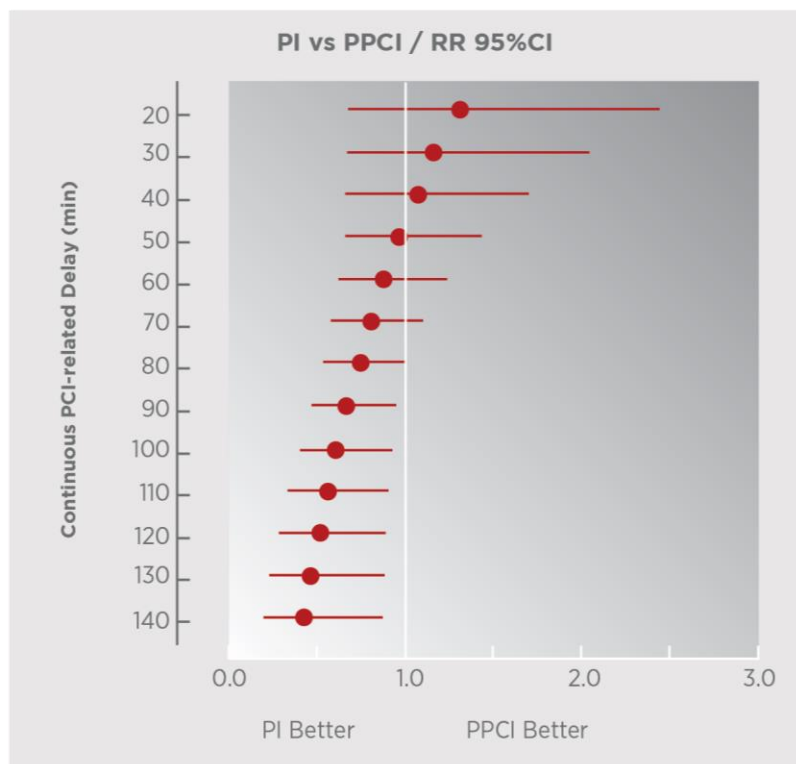
\* Death, congestive heart failure, cardiogenic shock, myocardial infarction  
PCI = Percutaneous Coronary Intervention;  
PPCI = Primary Coronary Intervention

Adapted from:

Gershlick AH, Westerhout CM, Armstrong PW, Huber K, Halvorsen S, Steg PG, Ostojic M, Goldstein P, Carvalho AC, Van de Werf F, Wilcox RG. Impact of a pharmaco-invasive strategy when delays to primary PCI are prolonged. Heart. 2015 May 1;101(9):692-8.



## STREAM: TIME DELAY



- Relative association of continuous PCI-related delay (min) and pharmaco-invasive treatment with 30-day composite outcome (CHF, shock, MI)

PI: Pharmaco-invasive; PPCI: primary percutaneous coronary intervention

Adapted from:

Gershlick AH, Westerhout CM, Armstrong PW, Huber K, Halvorsen S, Steg PG, Ostojic M, Goldstein P, Carvalho AC, Van de Werf F, Wilcox RG. Impact of a pharmaco-invasive strategy when delays to primary PCI are prolonged. Heart. 2015 May 1;101(9):692-8.



# STREAM: TIME DELAY

## CONCLUSIONS

---

- As **PCI-related delay (P-RD)** increased, pharmacoinvasive strategy outcomes became **superior to PPCI** when P-RD is prolonged and exceeds guideline-mandated times
- In such circumstances, a **pharmaco-invasive strategy** may provide an alternative reperfusion option
- Adverse **time delays for delivery of PPCI** should be considered when evaluating reperfusion strategies

PCI = Percutaneous Coronary Intervention; PPCI = Primary Coronary Intervention

Gershlick AH, Westerhout CM, Armstrong PW, Huber K, Halvorsen S, Steg PG, Ostojic M, Goldstein P, Carvalho AC, Van de Werf F, Wilcox RG. Impact of a pharmacoinvasive strategy when delays to primary PCI are prolonged. Heart. 2015 May 1;101(9):692-8.



## STREAM: ABORTED MI

**Evaluated the pre-specified STREAM endpoint, aborted MI, to compare a pharmaco-invasive strategy with PPCI**

	<b>Pharmaco-invasive strategy</b>	<b>PPCI</b>	
Aborted MI*	11.1%	6.9%	$p \leq 0.01$
Total ischaemic time**	90 mins	190 mins	-

\* Aborted MI is defined in the study as: “≥50% resolution in ST-elevation resolution in the ECG lead exhibiting the maximal baseline ST-elevation at either 90 min post-TNK or 30 min post- PCI in PI and primary PCI patients, respectively.” Additionally, biomarker analysis (either CK-MB  $\leq 2$  times the ULN or CK  $\leq 2$  times the ULN or cardiac troponin I/T (cTn) levels  $\leq 5$  times the ULN) was required.

\*\* Total ischaemic time for the pharmaco-invasive arm is defined as time from symptom onset to TNK and symptom onset to sheath insertion in the PPCI arm

TNK: tenecteplase; MI: myocardial infarction; PPCI: primary percutaneous coronary intervention;  
CK-MB: creatinine kinase MB isoenzyme; CK: creatinine kinase; ULN: Upper limit of normal

Adapted from:

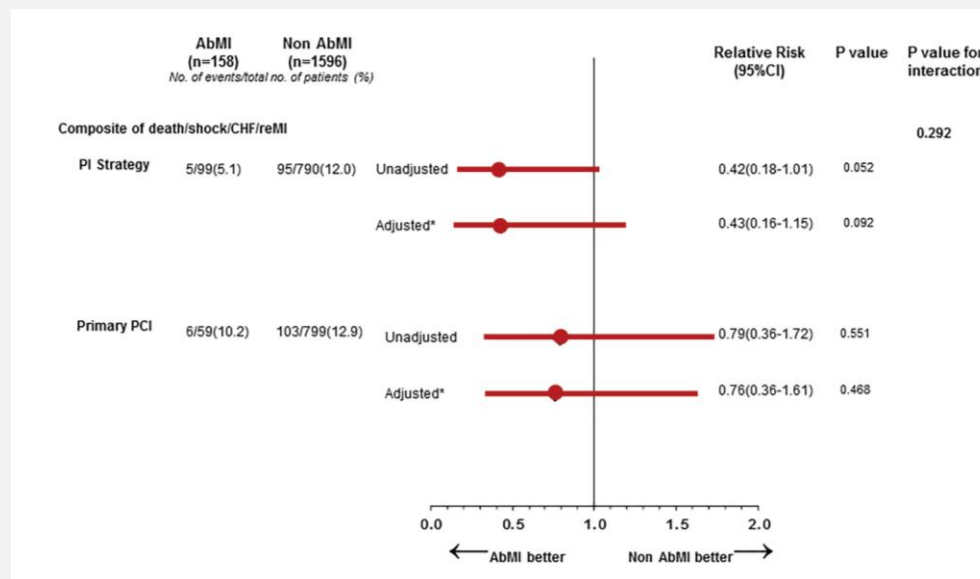
Maleki ND, Van de Werf F, Goldstein P, Adgey JA, Lambert Y, Sulimov V, Rosell-Ortiz F, Gershlick AH, Zheng Y, Westerhout CM, Armstrong PW. Aborted myocardial infarction in ST-elevation myocardial infarction: insights from the STrategic Reperfusion Early After Myocardial infarction trial. Heart. 2014 Oct 1;100(19):1543-9.





## STREAM: ABORTED MI

### Relative risk plot of the primary composite outcome and its components



\* Aborted MI is defined as “≥50% resolution in ST-segment elevation coupled with no or minimal subsequent rise in cardiac biomarkers and deemed to be an indicator of successful reperfusion therapy.”

Adapted from:

Maleki ND, Van de Werf F, Goldstein P, Adgey JA, Lambert Y, Sulimov V, Rosell-Ortiz F, Gershlick AH, Zheng Y, Westerhout CM, Armstrong PW. Aborted myocardial infarction in ST-elevation myocardial infarction: insights from the STrategic Reperfusion Early After Myocardial infarction trial. Heart. 2014 Oct 1;100(19):1543-9.



## STREAM: ABORTED MI

### CONCLUSIONS

---

- A **pharmaco-invasive strategy** of early fibrinolysis coupled with anti-thrombotic and antiplatelet therapy more frequently aborts MI than PPCI
- Such patients had more favourable outcomes **compared to non-AbMIs**



# STREAM: ECG INSIGHTS INTO STRATEGIC REPERFUSION

## Comparison of ECG metrics and clinical outcomes in three groups:

- **fibrinolysis requiring rescue angiography (n=348)**
- **fibrinolysis with scheduled angiography (n=516)**
- **PPCI (n=927)**

## % of patients with residual ST elevation $\pm 2$ mm 30 minutes after angiography:

Rescue patients	Scheduled patients	Primary PCI patients
27.9%	7.9%	24.8%

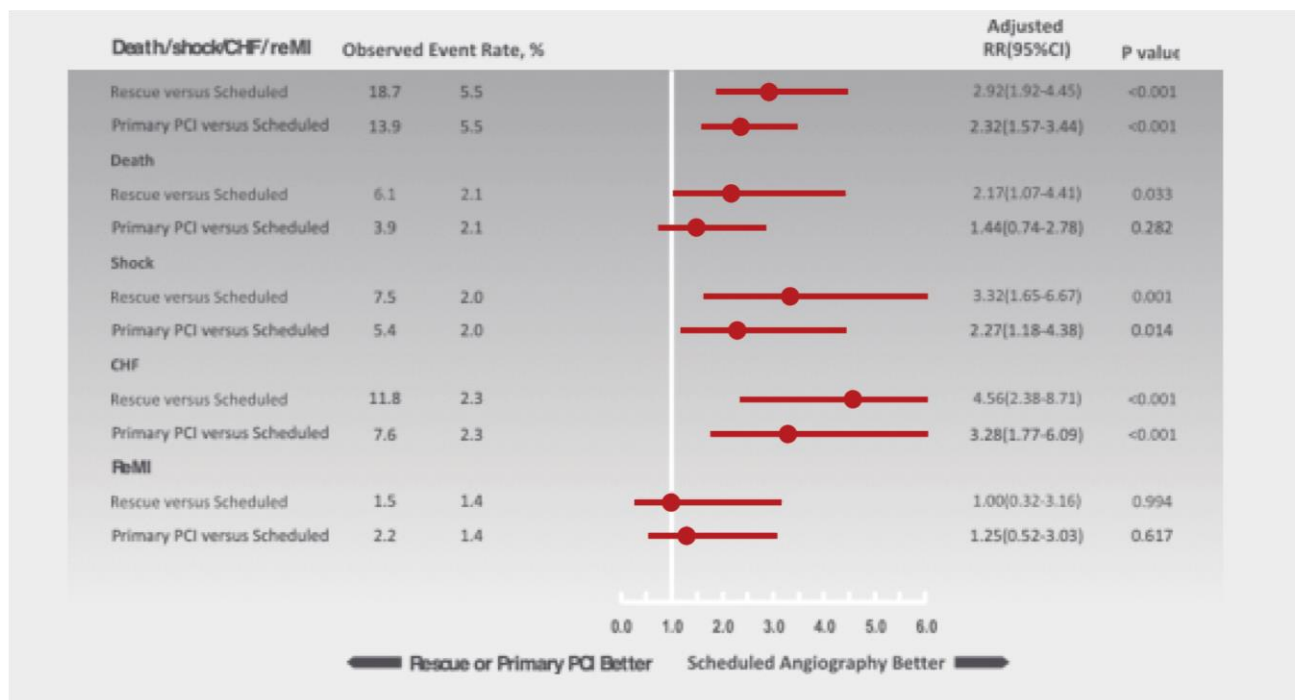
Adapted from:

Welsh RC, Van de Werf F, Westerhout CM, Goldstein P, Gershlick AH, Wilcox RG, Danays T, Bluhmki E, Lopes RD, Steg PG, Armstrong PW. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the STRategic Reperfusion Early After Myocardial Infarction [STREAM] study). The American journal of cardiology. 2014 Sep 15;114(6):811-9.



# STREAM: ECG INSIGHTS INTO STRATEGIC REPERFUSION

## REPERFUSION STRATEGY AND 30-DAY COMPOSITE ENDPOINT AND INDIVIDUAL CLINICAL EVENTS:



Adapted from:

Welsh RC, Van de Werf F, Westerhout CM, Goldstein P, Gershlick AH, Wilcox RG, Danays T, Bluhmki E, Lopes RD, Steg PG, Armstrong PW. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the STRategic Reperfusion Early After Myocardial Infarction [STREAM] study). The American journal of cardiology. 2014 Sep 15;114(6):811-9.



# STREAM: ECG INSIGHTS INTO STRATEGIC REPERFUSION

## CONCLUSIONS

---

- Fibrinolytic-treated patients not requiring rescue angiography had ECG evidence of **superior reperfusion** and lower clinical event rates than PPCI
- Patients requiring rescue angiography had higher risk with more **baseline co-morbidities** and worse 30-day outcomes

ECG: Electrocardiography; PPCI: primary percutaneous coronary intervention

Adapted from:

Welsh RC, Van de Werf F, Westerhout CM, Goldstein P, Gershlick AH, Wilcox RG, Danays T, Bluhmki E, Lopes RD, Steg PG, Armstrong PW. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the STRategic Reperfusion Early After Myocardial Infarction [STREAM] study). The American journal of cardiology. 2014 Sep 15;114(6):811-9.



## STREAM: ELDERLY PATIENTS

**Baseline characteristics, clinical outcomes, and relationship of TNK dose reduction to the efficacy, safety, and electrocardiographic indicators of reperfusion efficacy were evaluated in STEMI patients  $\geq 75$  years**

	<b>Pre-dose amendment patients (%)</b>	<b>Post-dose amendment patients (%)</b>
Median extent of ST-segment resolution ( $\geq 50\%$ )	63.2	56.0
$\geq 2$ mm in ECG lead with greatest ST-segment elevation	43.6	40.0
Rescue coronary intervention after TNK	42.9	44.1
Primary composite endpoint	31.0	24.7

TNK: tenecteplase; MI: myocardial infarction; ECG: Electrocardiography; STEMI: ST-Elevation Myocardial Infarction

Adapted from:

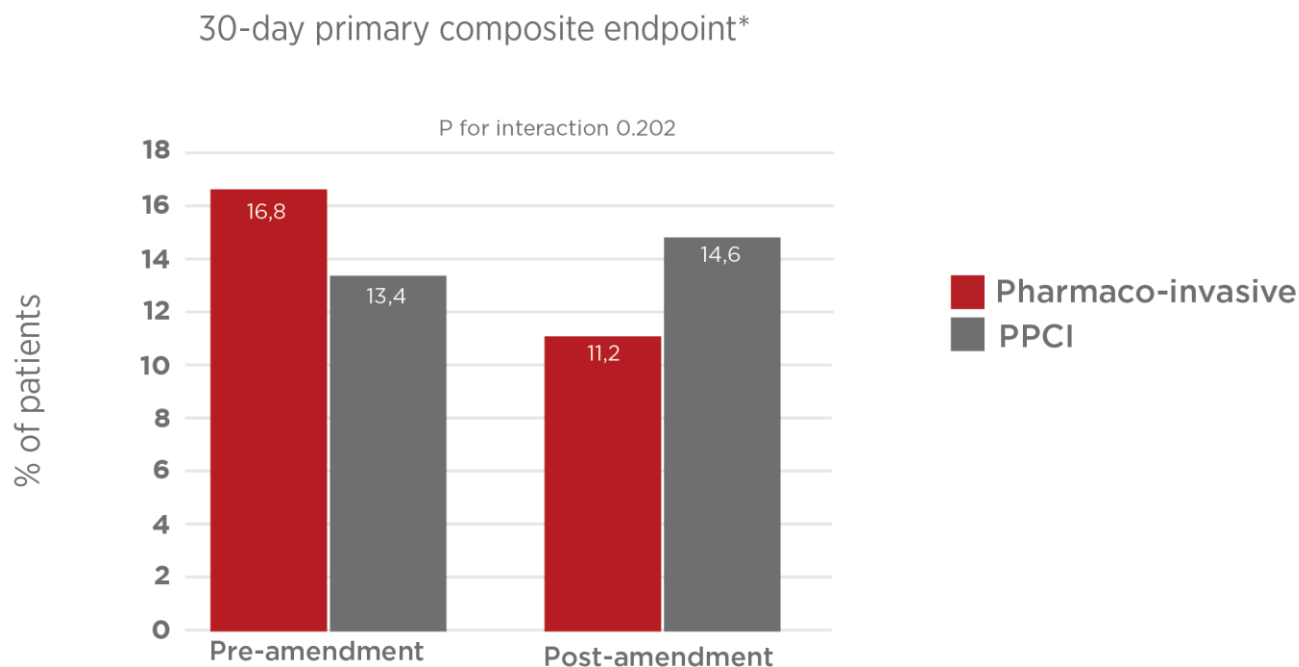
Armstrong PW, Zheng Y, Westerhout CM, Rosell-Ortiz F, Sinnaeve P, Lambert Y, Lopes RD, Bluhmki E, Danays T, Van de Werf F. Reduced dose tenecteplase and outcomes in elderly ST-segment elevation myocardial infarction patients: Insights from the STRategic Reperfusion Early After Myocardial infarction trial. American heart journal. 2015 Jun 1;169(6):890-8.





## STREAM: ELDERLY PATIENTS

### RELATIVE ASSOCIATION OF AMENDMENT AND STUDY TREATMENT WITH 30-DAY PRIMARY COMPOSITE END POINT:



\* 30-day all-cause death, cardiogenic shock, congestive heart failure, and re-infarction; PPCI: primary percutaneous coronary intervention;

Adapted from:

Armstrong PW, Zheng Y, Westerhout CM, Rosell-Ortiz F, Sinnaeve P, Lambert Y, Lopes RD, Bluhmki E, Danays T, Van de Werf F. Reduced dose tenecteplase and outcomes in elderly ST-segment elevation myocardial infarction patients: Insights from the STRategic Reperfusion Early After Myocardial infarction trial. American heart journal. 2015 Jun 1;169(6):890-8.



## STREAM: ELDERLY PATIENTS

### CONCLUSIONS

---

- Half-dose TNK reduces likelihood of **intracerebral haemorrhage** (ICH) without compromising reperfusion efficacy
- Observations are **hypothesis generating** and warrant further confirmation in randomised clinical trials in the elderly

TNK: tenecteplase

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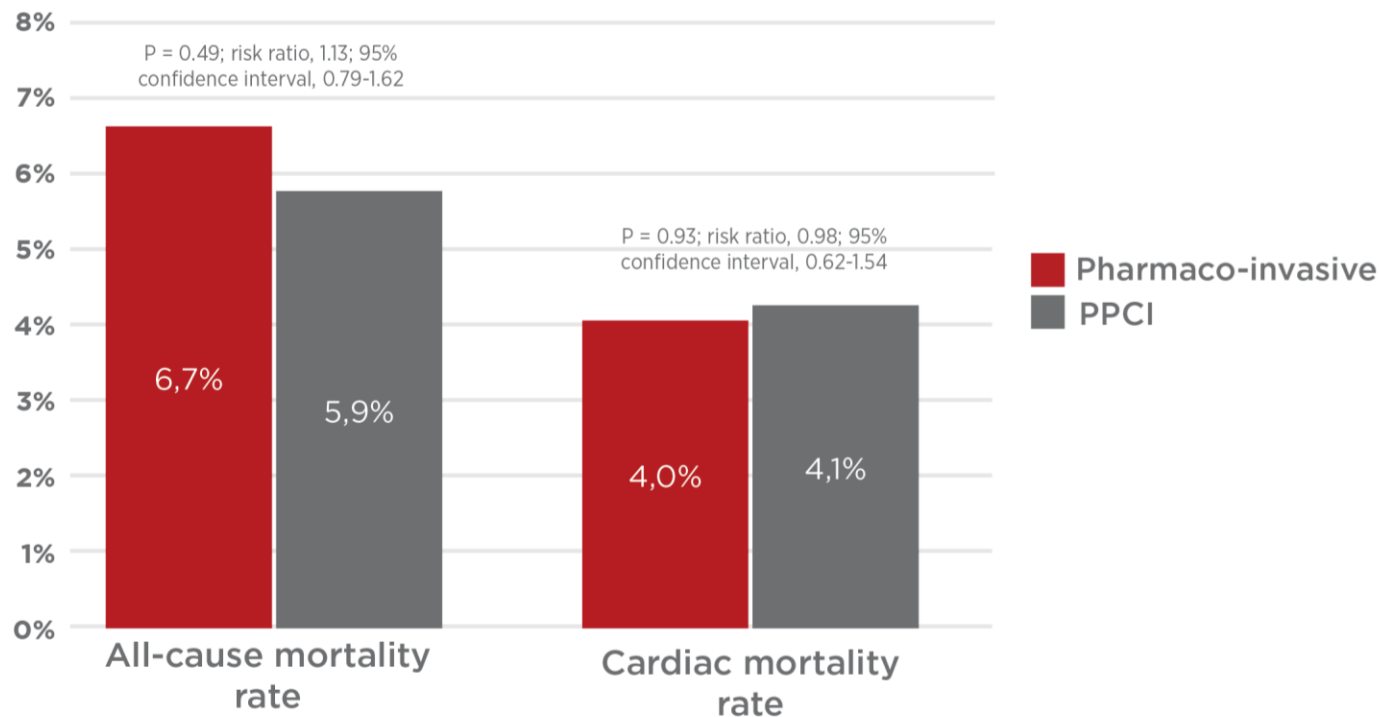
Armstrong PW, Zheng Y, Westerhout CM, Rosell-Ortiz F, Sinnaeve P, Lambert Y, Lopes RD, Bluhmki E, Danays T, Van de Werf F. Reduced dose tenecteplase and outcomes in elderly ST-segment elevation myocardial infarction patients: Insights from the STRategic Reperfusion Early After Myocardial infarction trial. American heart journal. 2015 Jun 1;169(6):890-8.



# STREAM: 1-YEAR MORTALITY FOLLOW-UP

## ALL-CAUSE AND CARDIAC MORTALITY RATES:

30-day primary composite endpoint\*



\* 30-day all-cause death, cardiogenic shock, congestive heart failure, and re-infarction; PPCI: primary percutaneous coronary intervention;

Sinnaeve PR, Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Lambert Y, Danays T, Soulat L, Halvorsen S, Ortiz FR, Vandenberghe K. St-segment-elevation Myocardial Infarction Patients Randomized to a Pharmaco-invasive Strategy or Primary Percutaneous Coronary Intervention: Strategic Reperfusion Early After Myocardial Infarction (stream) 1-year Mortality Follow-up. Circulation. 2014 Sep 30;130(14):1139-45.



## STREAM: 1-YEAR MORTALITY FOLLOW-UP

### CONCLUSIONS

At 1 year, mortality rates in the pharmaco-invasive strategy and PPCI arms were similar in STEMI patients presenting within 3h after symptom onset and unable to undergo PPCI within 1h

STEMI= ST segment elevation myocardial infarction; PPCI: primary percutaneous coronary intervention;

Sinnaeve PR, Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Lambert Y, Danays T, Soulat L, Halvorsen S, Ortiz FR, Vandenberghe K. St-segment-elevation Myocardial Infarction Patients Randomized to a Pharmaco-invasive Strategy or Primary Percutaneous Coronary Intervention: Strategic Reperfusion Early After Myocardial Infarction (stream) 1-year Mortality Follow-up. *Circulation*. 2014 Sep 30;130(14):1139-45.



## STREAM: CARDIAC RESULTS

1. **Pharmaco-invasive strategy** for early presenting STEMI nominally reduced 30-day cardiogenic shock and congestive heart failure compared with PPCI<sup>1</sup>
2. Evaluated whether this effect was associated with infarct size
  - Small ( $\leq 2$  times the upper limit normal [ULN])
  - Medium ( $> 2$  to  $\leq 5$  times the ULN)
  - Large ( $> 5$  times the ULN)

STEMI= ST segment elevation myocardial infarction; PPCI: primary percutaneous coronary intervention;  
ULN: Upper limit of normal

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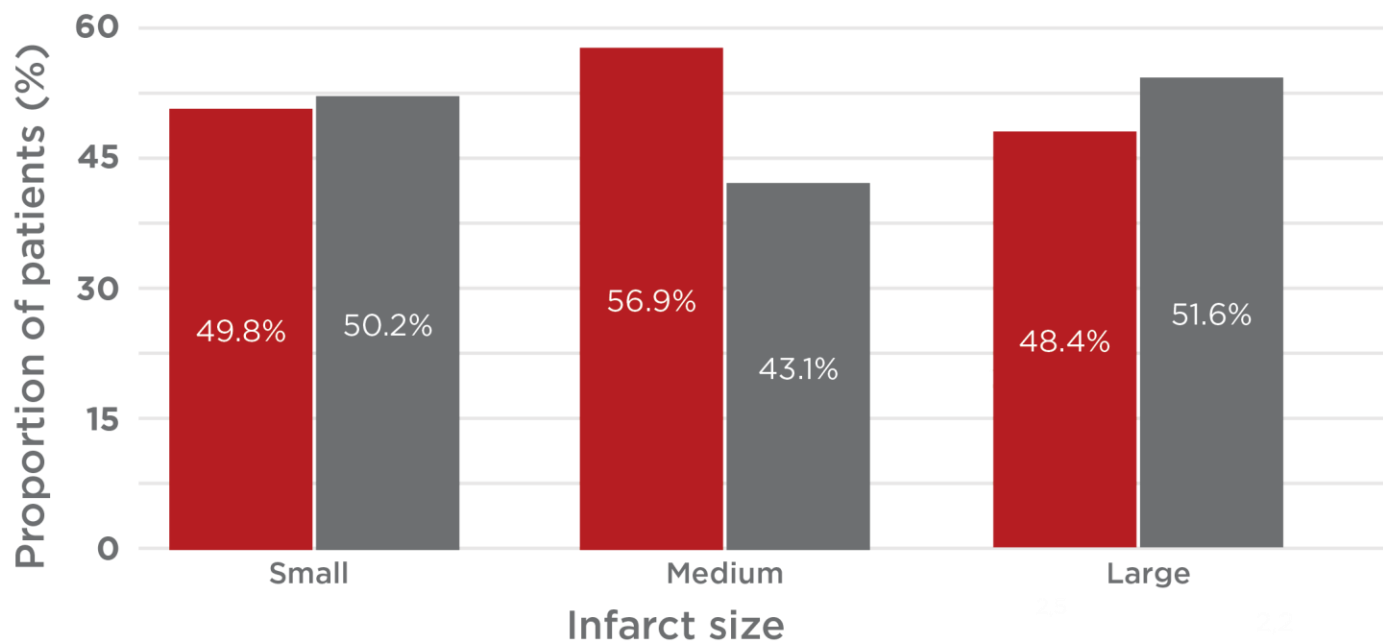
1. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.

2. Shavadia J, Zheng Y, Dianati Maleki N, Huber K, Halvorsen S, Goldstein P, Gershlick AH, Wilcox R, Van de Werf F, Armstrong PW. Infarct Size, Shock, and Heart Failure: Does Reperfusion Strategy Matter in Early Presenting Patients With ST-Segment Elevation Myocardial Infarction?. Journal of the American Heart Association. 2015 Aug 24;4(8):e002049.



## STREAM: CARDIAC RESULTS

■ Pharmaco-invasive  
■ PPCI



p=0.035 for different patient  
distribution across 3 groups

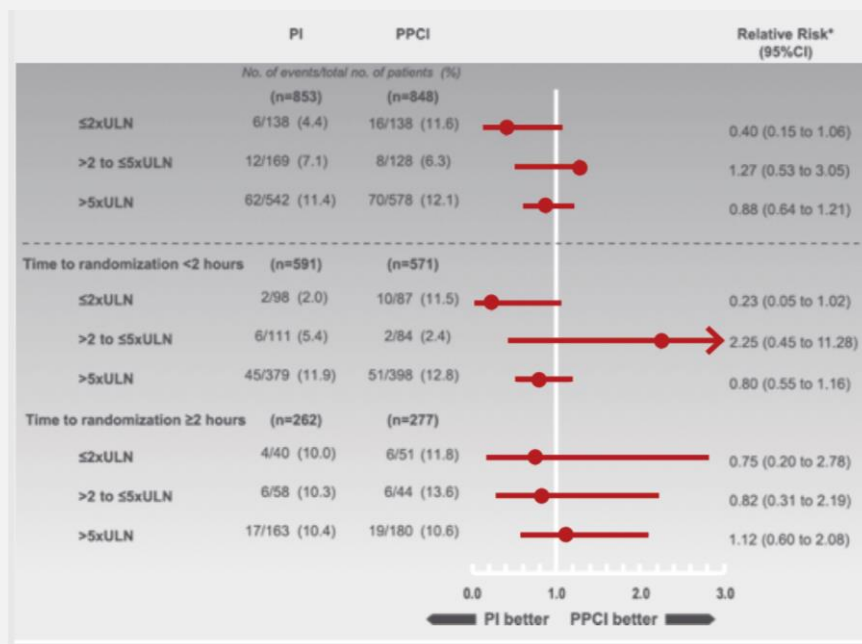
PPCI = Primary Percutaneous Coronary Intervention

1. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *New England Journal of Medicine*. 2013 Apr 11;368(15):1379-87.
2. Shavadia J, Zheng Y, Dianati Maleki N, Huber K, Halvorsen S, Goldstein P, Gershlick AH, Wilcox R, Van de Werf F, Armstrong PW. Infarct Size, Shock, and Heart Failure: Does Reperfusion Strategy Matter in Early Presenting Patients With ST-Segment Elevation Myocardial Infarction?. *Journal of the American Heart Association*. 2015 Aug 24;4(8):e002049.



# STREAM: CARDIAC RESULTS

## Relative risk plot of the 30-day composite endpoint of shock/congestive heart failure (CHF)



**Upper panel:**  
infarct size groups and  
30-day shock/CHF by  
treatment strategy

**Lower panel:**  
infarct size groups and  
30-day shock/CHF by  
treatment strategy and  
pre-specified 2-hour time  
from symptom onset to  
treatment randomisation  
cut-off

\* Adjusted for thrombolysis in myocardial infarction risk score

1. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *New England Journal of Medicine*. 2013 Apr 11;368(15):1379-87.
2. Shavadia J, Zheng Y, Dianati Maleki N, Huber K, Halvorsen S, Goldstein P, Gershlick AH, Wilcox R, Van de Werf F, Armstrong PW. Infarct Size, Shock, and Heart Failure: Does Reperfusion Strategy Matter in Early Presenting Patients With ST-Segment Elevation Myocardial Infarction?. *Journal of the American Heart Association*. 2015 Aug 24;4(8):e002049.



# STREAM: CARDIAC RESULTS

## CONCLUSIONS

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- A **pharmaco-invasive strategy** appears to alter the pattern of infarct size after STEMI, resulting in **more medium and fewer large infarcts** compared with PPCI
- Despite a comparable number of small infarcts, pharmaco-invasive strategy patients in this group had **more aborted myocardial infarctions** and less 30-day shock and congestive heart failure

PPCI = Primary Percutaneous Coronary Intervention; STEMI= ST segment elevation myocardial infarction

1. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. New England Journal of Medicine. 2013 Apr 11;368(15):1379-87.
2. Shavadia J, Zheng Y, Dianati Maleki N, Huber K, Halvorsen S, Goldstein P, Gershlick AH, Wilcox R, Van de Werf F, Armstrong PW. Infarct Size, Shock, and Heart Failure: Does Reperfusion Strategy Matter in Early Presenting Patients With ST-Segment Elevation Myocardial Infarction?. Journal of the American Heart Association. 2015 Aug 24;4(8):e002049.





# STREAM-2 (STRATEGIC REPERFUSION IN ELDERLY PATIENTS AFTER MYOCARDIAL INFARCTION)

## THE AIM IS TO COMPARE THE EFFICACY AND SAFETY OF

- **EARLY FIBRINOLYTIC TREATMENT**  
(half-dose TNK and antiplatelet therapy) followed by catheterisation within **6-24 hours or rescue PCI** if indicated versus
- **PPCI**  
in **elderly patients (≥70 years)** with STEMI treated within 3h of symptom onset

### COMPOSITE ENDPOINT:

death, shock, heart failure, recurrent MI at 30 days

### TRIAL STATUS:

Using a study design similar to STREAM, STREAM 2 started 01 August 2017 with an estimated completion date of June 2020

PCI = Percutaneous Coronary Intervention; STEMI= ST segment elevation myocardial infarction

Clinicaltrials.gov identifier: NCT02777580.