Nitric Oxide for Inhalation to Reduce Reperfusion Injury in STEMI - NOMI

*Stefan P. Janssens, MD, PhD on behalf of the **NOMI investigators**:*

K.D. Bloch, MD, J. Bogaert, MD, PhD, B. Merkely, MD, PhD,

F. Van de Werf, MD, PhD, P. Vranckx, MD, PhD, J. Zalewski, MD, PhD

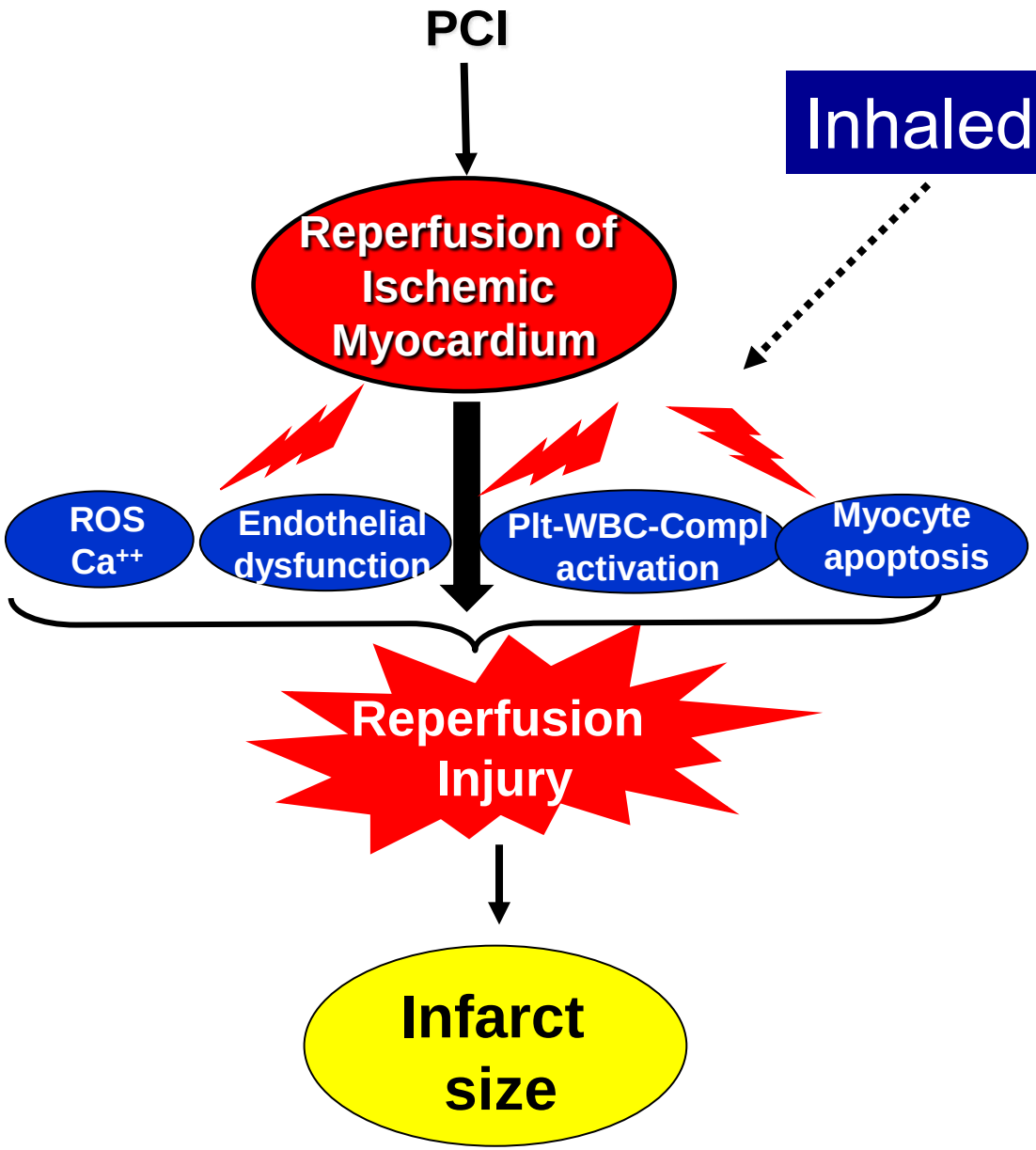
Krakowski Szpital Specjalistyczny im. Jana Pawła II

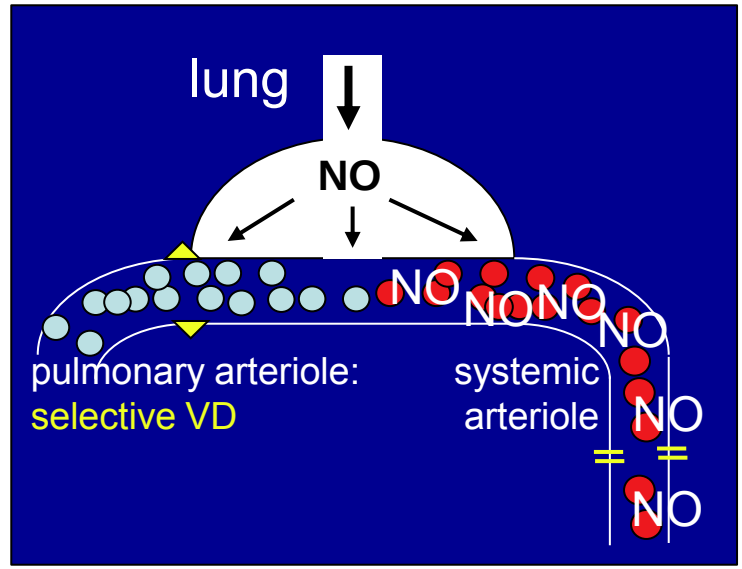
Hartcentrum Hasselt

DECLARATION OF INTEREST

Research contract: preclinical study in pigs

Inhaled NO for Cardioprotection during Ischemia





- Inhalation of 40 and 80 ppm NO for 24h reduced IS/AAR in mice
  (*Hataishi R et al. AJ P Heart Circ Physiol. 2006; Nagasaka Y et al. Anesthesiology. 2008)*

- Inhalation of 80 ppm NO for 4h reduced IS/AAR and improved functional recovery in pigs, while 2 ug/kg/min IV NTG failed to do so.
  (X. Liu et al. JACC 2007)

NOMI: hypothesis and design

- In STEMI patients with successful percutaneous coronary intervention (PCI), inhalation of NO reduces infarct size (IS), and improves LV functional and structural recovery.
- **Phase II, multicentre, double-blind, RCT**

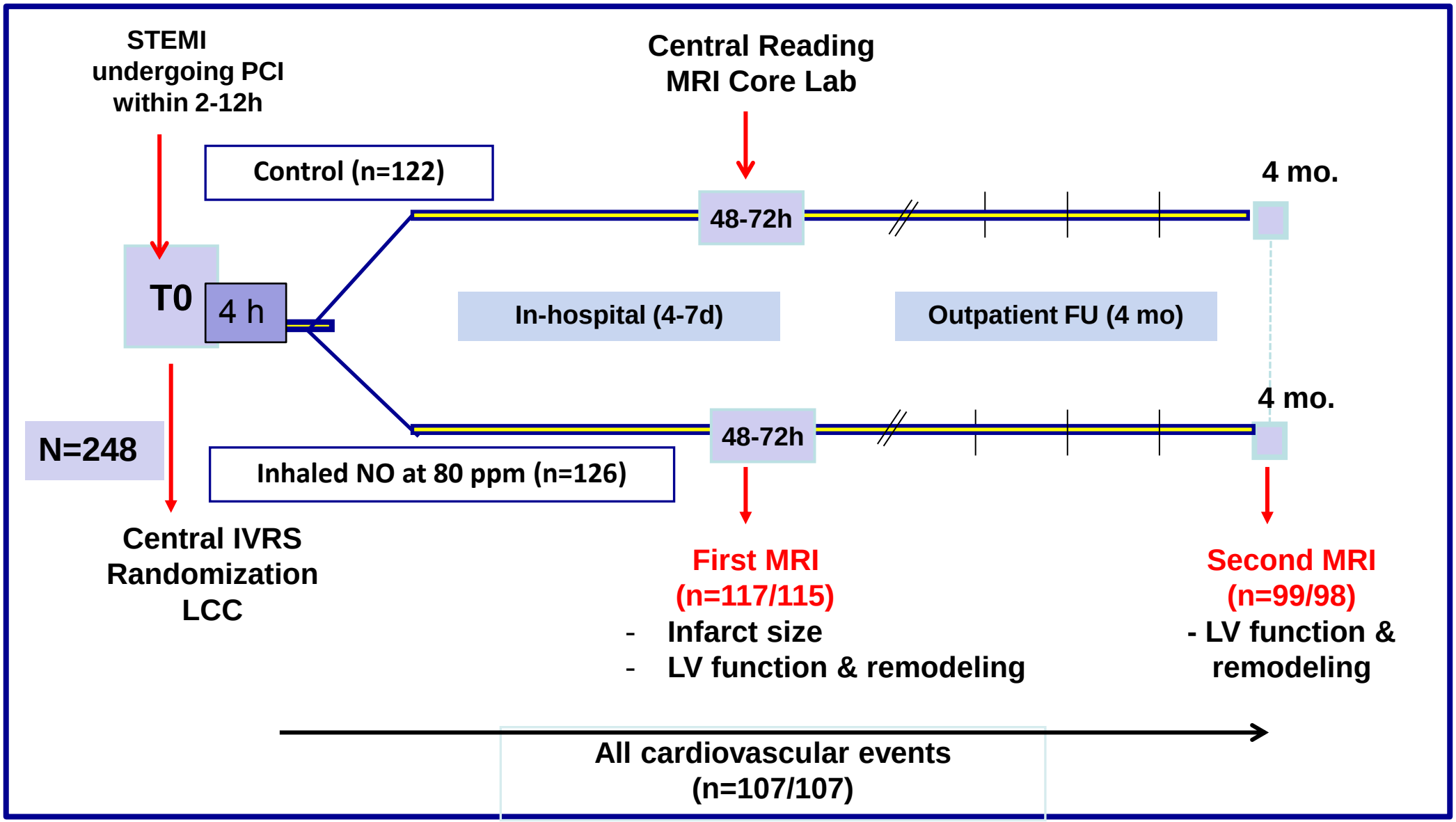
- **Inclusion criteria:**
  - presenting within 2-12 h of first STEMI
  - no heart failure or abnormal O_2 sat
  - signed informed consent

Pre-specified subgroups for primary EP:

- TIMI flow grade
- Culprit lesion: LAD vs non-LAD
- Time symptom onset to PCI < or > 6h
- Troponin level on admission

- **Use of systemic nitroglycerin (IA/IC)**
- **Use of glycoprotein IIb/IIIa antagonists**

NOMI: Study design

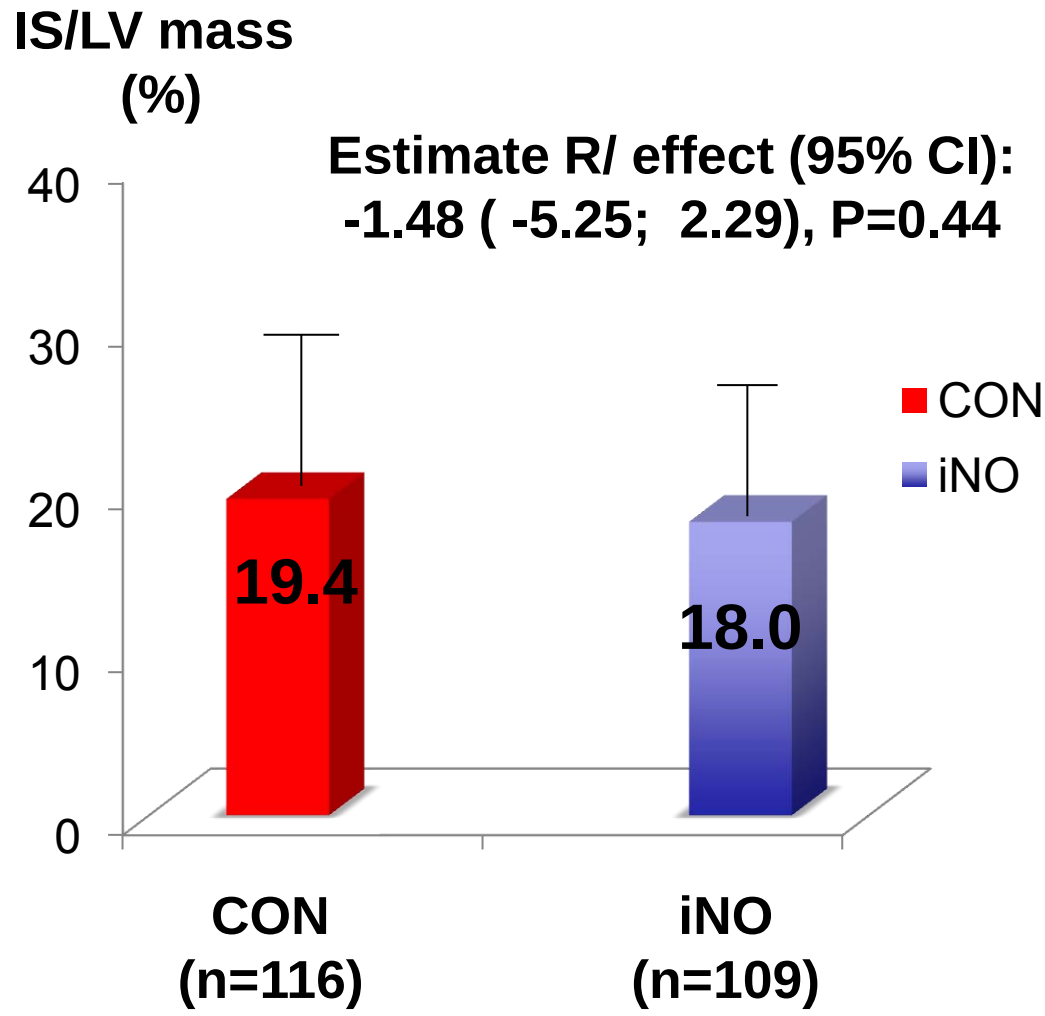


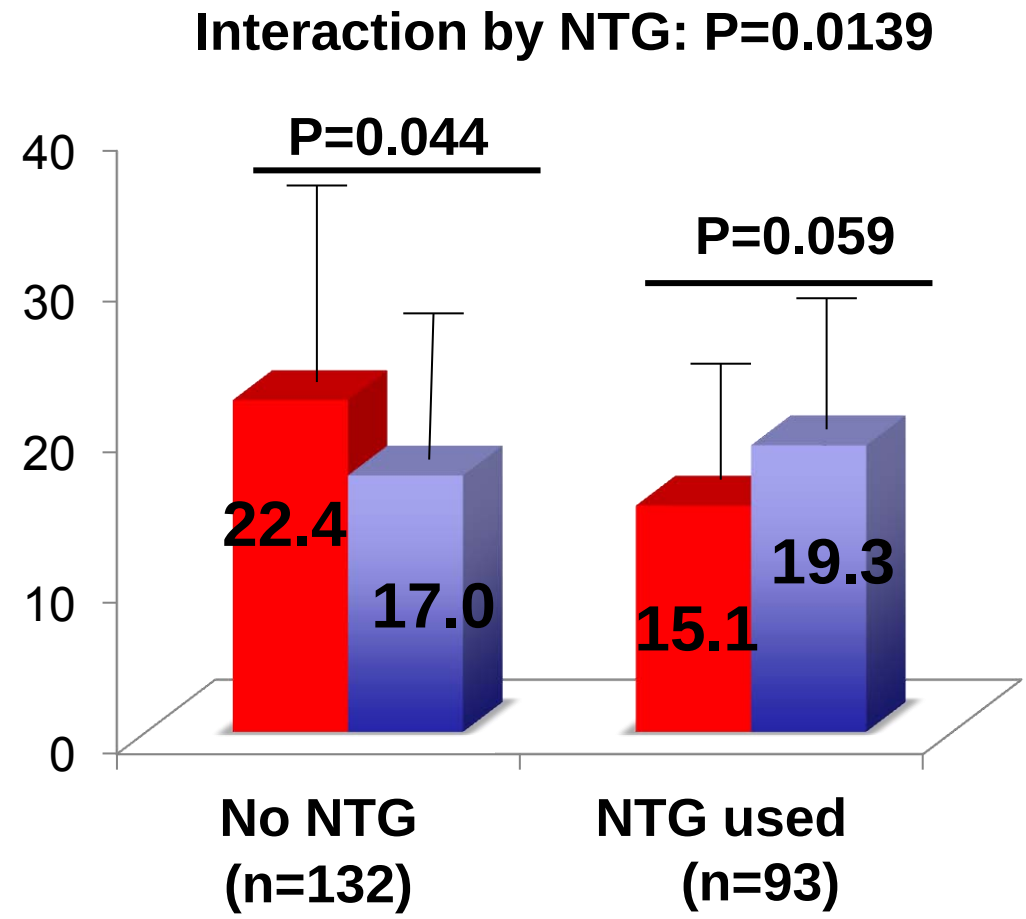
NOMI Baseline and Procedural characteristics (Full Analysis Set)

	iNO (n=122)	CON (n=127)	P-value
Age (mean, SD)	63 (13)	60 (11)	0.19
Female n(%)	44 (36)	33 (26)	0.09
Hypertension n(%)	75 (61)	72 (57)	0.44
Hyperlipidaemia n(%)	55 (45)	60 (47)	0.73
Type 2 Diabetes n(%)	15 (12)	13 (10)	0.61
Current smoker n(%)	57 (47)	56 (44)	0.76
Time from symptom to Tx, (mean,SD) (h)	4.4±2.5	4.5±2.8	0.91
TIMI grade 0-1 pre PCI, n(%)	83 (68)	89 (70)	0.68
Anterior location, n(%)	52 (43)	55 (43)	0.66
IA/IC NTG use, n(%)	**56 (46)**	**60(47)**	0.89
GP IIb/IIIa use, n(%)	**48 (39)**	**54 (43)**	0.69
Methemoglobin (%)	1.06 (0.41)	0.68 (0.31)	-

(no treatment related clinical adverse event during study drug administration)

NOMI: Treatment effect of inhaled NO on relative Infarct Size in STEMI



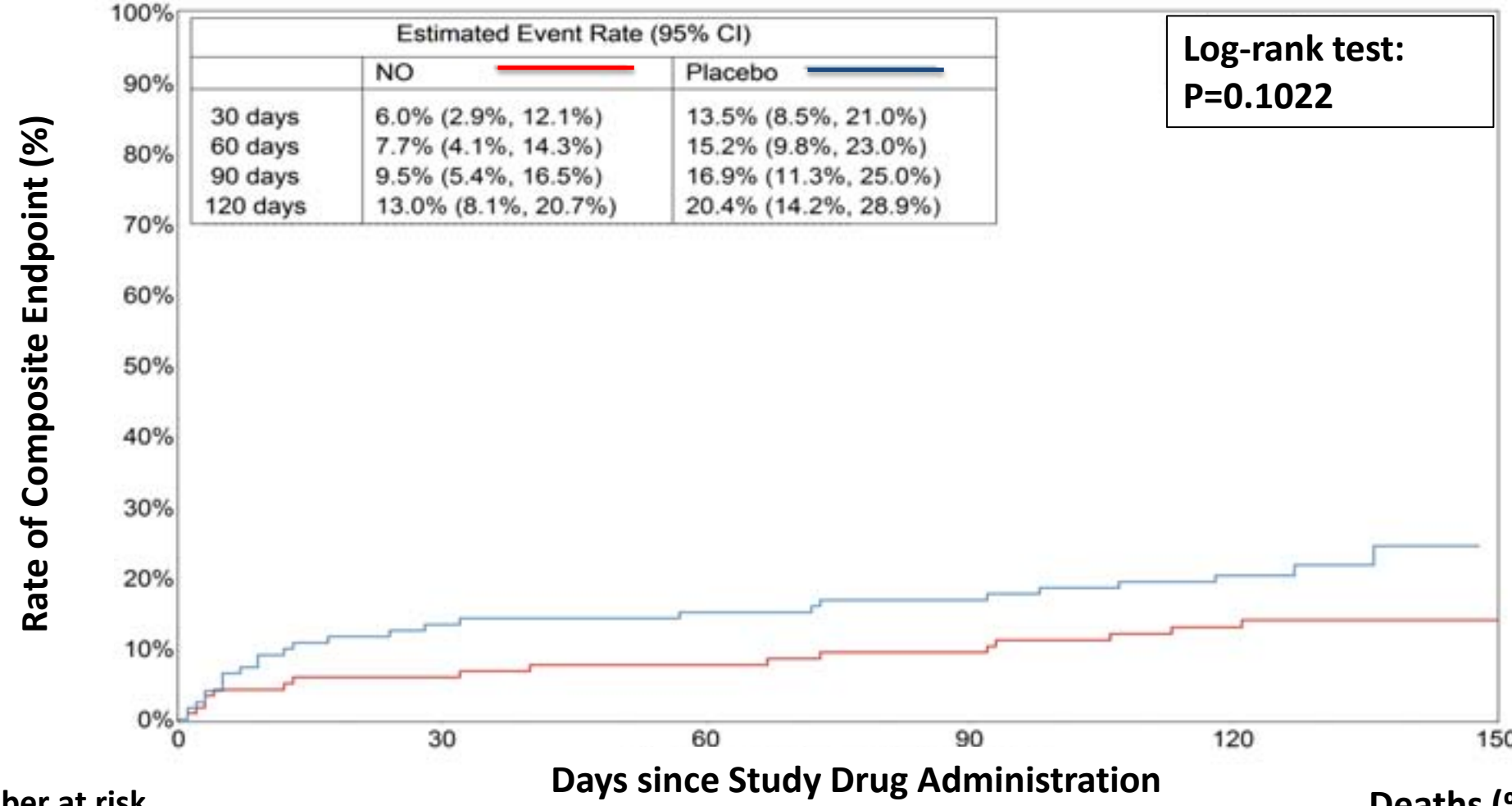


NOMI: secondary CMR endpoints at 48-72h and 4 mo

	NO Mean (sd)	CON Mean (sd)	Effect size: estimates or Odds Ratio (95% CI)	P-value
Secondary EP:				
- IS/Area at risk (%)	53 (26)	60 (26)	-6.8 (-14.8, 1.3)	**0.09**
- Myocardial salvage index (%)	47 (26)	40 (26)	6.8 (-1.3, 14.8)	**0.09**
- Myocardial haemorrhage n (%)	14 (13)	23 (21)	0.58 (0.28, 1.20)	**0.14**
LV remodeling 48-72h				
- LV-ESVi (mL/m^2)	41 (14)	44 (18)	0.93 (0.85, 1.02)	**0.10**
- LV-EDVi (mL/m^2)	79 (16)	82 (19)	0.97 (0.91, 1.02)	**0.21**
LV remodeling 4 mo				
- LV-ESVi (mL/m^2)	41 (16)	46 (21)	0.898 (0.807, 0.999)	**0.048**
- LV-EDVi (mL/m^2)	84 (18)	90 (22)	0.943 (0.886, 1.003)	**0.063**

NOMI: Kaplan-Meier for Composite Endpoint

(death, recurrent ischemia, stroke or rehospitalization)



Number at risk

						Deaths (%)
NO	119	109	106	104	97	5 (4.1)
CON	125	101	99	97	91	8 (6.3)

Summary and Conclusions: NO for Inhalation in Myocardial Infarction

- In timely reperfused STEMI, inhalation of NO on top of standard treatment was safe but did not reduce infarct size expressed as % LV mass.
- In a pre-specified subgroup analysis, we found statistically significant heterogeneity of the iNO effect on IS in relation to periprocedural NTG use. iNO reduced infarct size in NTG naïve patients (P = 0.044), whereas it increased IS in patients that received NTG during the procedure.
- Inhaled NO showed a trend towards greater myocardial salvage index, and enhanced functional recovery, which was more accentuated over time.

- Our data suggest that iNO might reduce infarct size in NTG naïve patients. This pre-specified subgroup finding, together with a robust safety profile and promising clinical trends, needs independent corroboration in future studies.