Table 1. AVOID Study Procedural Details

	Oxygen (n = 218)	No Oxygen (n = 223)
Radial access	33.2	33.3
Stent implanted	92.7	90.1
Drug-eluting stent	51.4	51.1
Glycoprotein IIb/IIIa inhibitor	44.5	40.4
Thrombus aspiration	49.1	47.1
Intra-aortic balloon pump	3.2	5.4
Coronary artery bypass graft	2.3	4.0
No revascularization	5.0	5.9
Symptom to intervention time, min	150.5 (125.0, 213.8)	162.0 (130.0, 240.0)
Door to intervention time, min	54.0 (39.0, 66.3)	56.0 (42.0, 70.8)

Values are given in percentages or median (interquartile range).
AVOID, Air Versus Oxygen in Myocardial Infarction.
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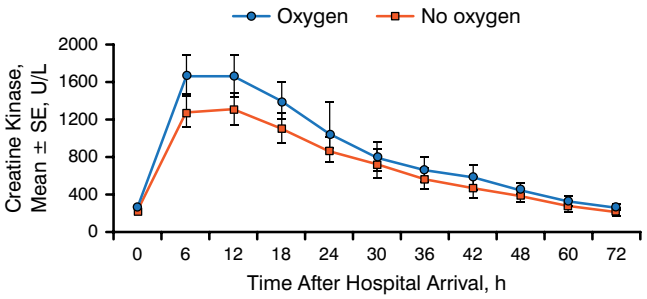
Figure 1. Creatine Kinase Values in the Study Groups

Creatine kinase, U/L	Oxygen (n = 217)	No oxygen (n = 222)	Ratio of means (oxygen/ no oxygen)	*P* Value
Geometric mean peak (95% CI)	1948 (1721 to 2205)	1543 (1341 to 1776)	1.26 (1.05 to 1.52)	.01
Median peak (IQR)	2073 (1065, 3753)	1727 (737, 3598)		.04



Area under the curve, *P* = .04.
IQR, interquartile range.
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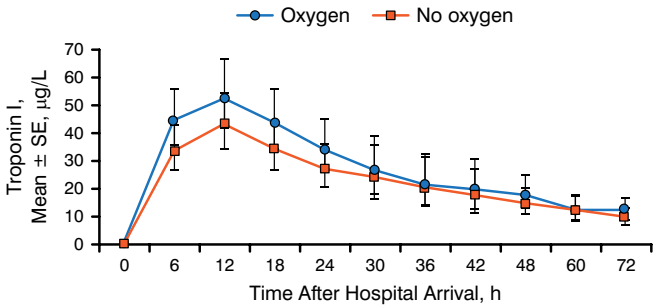
was similar, but the groups were not significantly different (Figure 2).

MRI was conducted at 6 months in 65 patients who had received oxygen and 74 patients who had received no oxygen. This revealed a trend toward increased cardiac infarct size as a proportion of left ventricle mass, indicative of scarring, between the oxygen and no-oxygen arms (12.6%; 6.7 to 19.2% vs 9.0%; 4.1 to 16.3%; *P* = .08).

The trial was underpowered to assess clinical end points; thus, all findings are considered exploratory.

Figure 2. Troponin Values in the Study Groups

Troponin I, µg/L	Oxygen (n = 200)	No oxygen (n = 205)	Ratio of means (oxygen/no oxygen)	*P* Value
Geometric mean peak (95% CI)	57.4 (48.0 to 68.6)	48.0 (39.6 to 58.1)	1.20 (0.92 to 1.55)	.18
Median peak (IQR)	65.7 (30.1, 145.1)	62.1 (19.2, 144.0)		.17



Area under the curve, *P* = .12.
IQR, interquartile range.
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Supplemental oxygen use was associated with recurrent MI at hospital discharge (5.5% vs 0.9%). The trend continued to 6 months, although the result was less impressive (7.6% vs 3.6%). There was an association between MACCEs at 6 months in the oxygen arm (21.9% vs 15.4%). Mortality was low in both the oxygen and no-oxygen arms (3.8% vs 5.9% at 6 months).

The use of oxygen in STEMI patients was associated with greater myocardial injury, as assessed by creatine kinase (but not troponin), with a suggestion of increased recurrent MI and major cardiac arrhythmia and larger myocardial infarct size at 6 months. The findings question the current practice of supplying oxygen to all patients with MI.

PARADIGM-HF: Disease Progression Slowed With Novel Drug

Written by Mary Mosley

The first-in-class angiotensin receptor neprilysin inhibitor LCZ696—compared with the gold standard treatment of enalapril—significantly reduced the composite primary outcome of cardiovascular (CV) death or heart failure (HF) hospitalization in patients with HF and reduced ejection fraction in the prospective trial Efficacy and Safety of LCZ696 Compared With Enalapril on Morbidity and Mortality of Patients With Chronic Heart Failure [PARADIGM-HF; McMurray JJ

et al. *N Engl J Med*. 2014]. The components of the primary outcome, as well as the secondary outcome of all-cause mortality, were also significantly reduced.

New results from analyses of prespecified outcomes showed that HF progression is attenuated and fatal and that nonfatal worsening heart failure (WHF) is delayed or prevented with LCZ696 when compared with enalapril, according to John J. V. McMurray, MD, University of Glasgow, Glasgow, Scotland, UK. LCZ696 combines a neprilysin inhibitor prodrug (sacubitril) and the angiotensin receptor blocker valsartan, thereby blocking both the AT_1 receptor and inhibiting the enzyme neprilysin, which breaks down natriuretic peptides and other vasoactive substances with beneficial effects in HF, to obtain incremental benefits beyond blockade of the renin angiotensin system alone.

In the original study, the median follow-up was 27 months, and the average daily dose at the last visit was LCZ696, 375 mg, and enalapril, 18.9 mg. The patients were aged 63.8 years; 22% were women; 60% had ischemic cardiomyopathy; and the mean left ventricular ejection fraction was about 29%.

Based on patient and physician assessments, the proportion of patients with WHF at month 8 was lower with LCZ696 vs enalapril [Packer M et al. *Circulation*. 2014]. For each domain measured by the Kansas City Cardiomyopathy Questionnaire, fewer patients in the LCZ696 group reported ≥5 points in deterioration (level considered to be clinically meaningful). Regarding change in NYHA class from baseline, more patients in the LCZ696 group improved (16.7% vs 14.9% with enalapril; $P=.0015$), and fewer patients progressed to a higher NYHA class (5.4% vs 7.0%, respectively), while 78% of each group had no change.

LCZ696 had a favorable influence on a number of parameters that are a measure of WHF—including reductions in treatment failure (as measured by the need for treatment intensification), emergency department visits for HF, hospitalization for HF, intensive care unit admission, and use of inotropic drugs (Table 1).

The need for devices, ventricular assist devices, or heart transplant for WHF was numerically lower with LCZ696 vs enalapril (Table 2).

Notably, all-cause hospitalization was reduced with LCZ696 as compared with enalapril, at about 110 fewer hospitalizations per 1000 patients, stated Prof McMurray. The number of admissions for any cause, including repeat episodes, was reduced (RR, 0.84; 95% CI, 0.78 to 0.91; $P<.001$), as was the proportion of patients hospitalized (HR, 0.88; 95% CI, 0.82 to 0.94; $P<.001$).

The rate of death for WHF was lower with LCZ696 vs enalapril (HR, 0.79; $P=.34$) and was significant for all-cause death (HR, 0.84; $P<.001$), CV death (HR, 0.80; $P=.00008$), and sudden death (HR, 0.80; $P=.008$).

Table 1. Effect of Enalapril and LCZ696 on Outcomes Associated With Heart Failure Progression

	Enalapril (n = 4212)	LCZ696 (n = 4187)	HR (95% CI)	*P* Value
Treatment intensification, %	14.3	12.4	0.84 (0.74 to 0.94)	.003
Patients with HF ED visit, %	3.6	2.4	0.66 (0.52 to 0.85)	.001
ED visits for HF, no.	208	151	0.70 (0.52 to 0.94)[a]	.017
Patients hospitalized for HF, %	15.6	12.8	0.79 (0.71 to 0.89)	< .001
Hospitalizations for HF, no.	1079	851	0.77 (0.67 to 0.89)[a]	< .001
Patients requiring ICU, no.	623	549	0.87 (0.78 to 0.98)	.019
ICU stays, no.	879	768	0.82 (0.72 to 0.94)[a]	.005
IV inotropic drugs in ICU, %	5.4	3.9	0.69 (0.57 to 0.85)	< .001

ED, emergency department; HF, heart failure; ICU, intensive care unit; IV, intravenous.

[a]Rate ratio.

Source: Packer M et al. *Circulation*. 2014.

Table 2. Rate of Device Implantation, Ventricular Assist Device Insertion, and Transplant for Worsening Heart Failure

	LCZ696 (n = 4187)	Enalapril (n = 4212)	*P* Value
CRT-D	54 (1.3)	77 (1.8)	.052
CRT-P	34 (0.8)	31 (0.7)	.710
VAD	12 (0.29)	19 (0.45)	.280
Transplant	1 (0.02)	4 (0.09)	.375

Data are presented as no. (%).

CRT-D, cardiac resynchronization therapy with defibrillator; CRT-P, cardiac resynchronization therapy with pacemaker; VAD, ventricular assist device.

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PreSERVE-AMI: CD34+ Cells Improve Cardiac Function, Reduce Events After STEMI

Written by Mary Mosley

The intracoronary (IC) infusion of bone marrow mononuclear cells after an STEMI improved cardiac function, including left ventricular ejection fraction (LVEF), infarct size, and end-systolic volume, and major adverse cardiac events (MACEs) [Huikuri HV et al. *Eur Heart J*. 2008; Martin-Rendon E et al. *Eur Heart J*. 2008; Schachinger V et al. *N Engl J Med*. 2006]. A phase 1 study