

Iso-osmolar vs. low-osmolar  
contrast medium in patients with impaired  
renal function undergoing PCI

## CONTRAST

(Contrast media and NephroToxicity following coronary  
Revascularization by Angioplasty)

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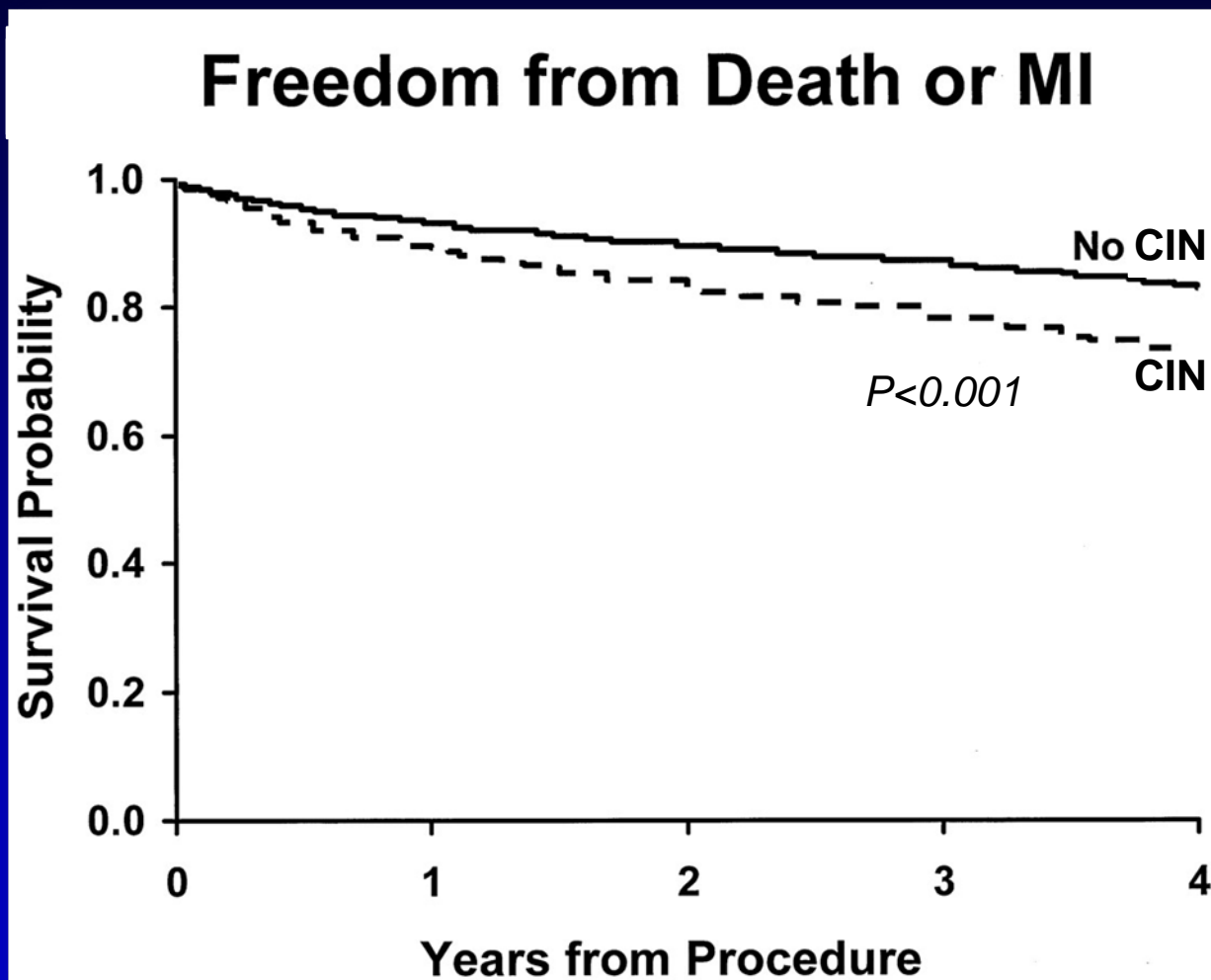
## Disclosures

This trial was supported in part by GE Healthcare Buchler.

*The company did not participate in the design and conduct of the study, in the collection, analysis and interpretation of the data, or in the preparation, review, or approval of this presentation.*

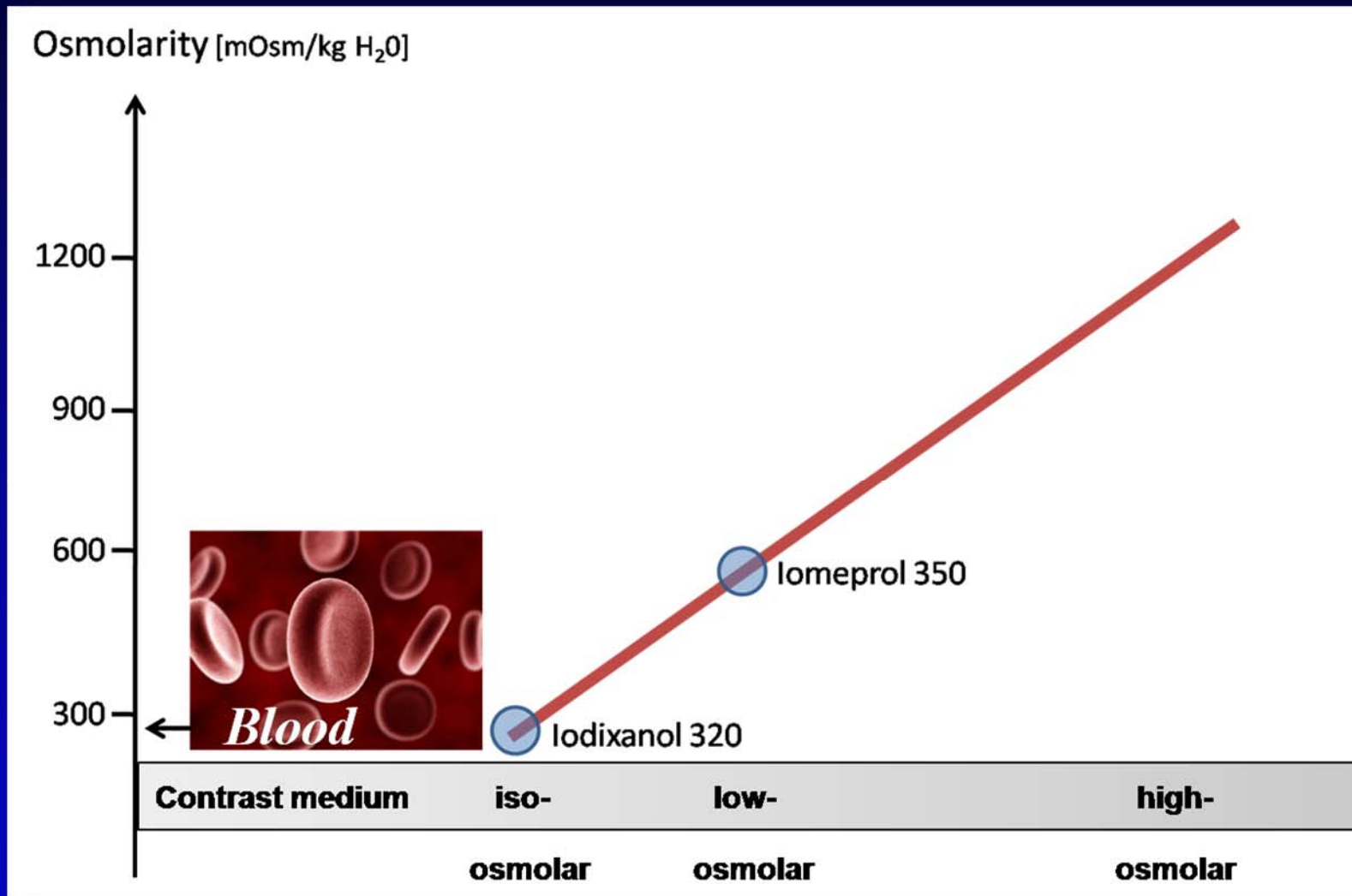
# Background

- Patients with chronic renal failure (CRF) have an increased incidence of coronary artery disease.
- In these high risk patients, PCI is often complex and associated with increased application of contrast medium.
- However, patients with CRF are at increased risk for contrast medium induced nephropathy (CIN) that is associated with adverse outcomes.
- Therefore, a strategy to reliably decrease the incidence of CIN following PCI in these high risk patients is warranted.



CIN defined as increase of S-creatinine  $\geq 0.5$  mg/dl

Rihal CS et al., Circulation 2002



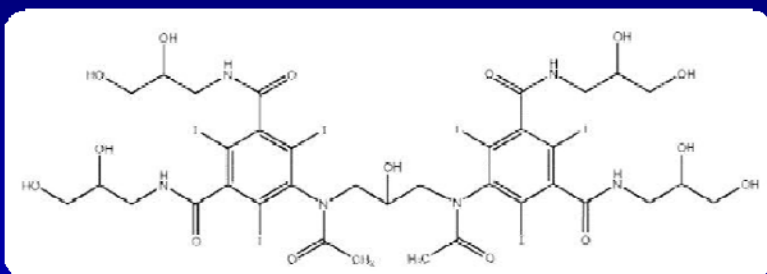
- Conflicting study results about the effect of LOCM vs. IOCM regarding CIN in cardioangiography (e.g. NEPHRIC vs. CARE, etc.)
- No dedicated randomized trial available evaluating contrast mediated nephrotoxicity in patients with renal dysfunction undergoing PCI that receive high volumes of either LOCM or IOCM.



# Aim of the **CONTRAST** study

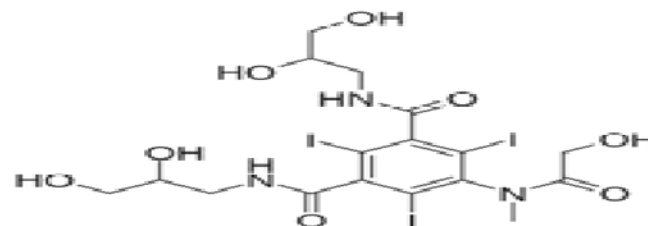
To compare nephrotoxicity between the  
iso-osmolar contrast medium (IOCM) **IODIXANOL**  
and the  
low-osmolar contrast medium (LOCM) **IOMEPROL**  
in patients with impaired renal function undergoing PCI.

## IODIXANOL 320



- Osmolarity: 290 mosm/kg H<sub>2</sub>O  
→ categorized as “**iso-osmolar**”
- Nonionic dimer
- 320 mg iodine per ml

## IOMEPROL 350



- Osmolarity: 618 mosm/kg H<sub>2</sub>O  
→ categorized as “**low-osmolar**”
- Nonionic monomer
- 350 mg iodine per ml

## STUDY HYPOTHESIS:

In patients with impaired renal function undergoing PCI, Iodixanol 320 imposes less nephrotoxicity compared to Iomeprol 350

## SAMPLE SIZE CALCULATION:

- assumption (based on literature): mean rise in S-creatinine levels after PCI in pts. with CRF  $\approx 0.4$  mg/dl
- Increase in S-creatinine can be reduced by Iodixanol by  $\geq 25\%$
- test significance level  $\alpha = 0.05$
- ➔ n per group: 143
- ➔ 324 patients enrolled to accommodate for possible dropouts

## Primary endpoint:

Rise of S-creatinine as a measure of contrast medium induced nephrotoxicity during hospitalization for PCI

## Secondary endpoints:

- Duration of hospitalization
- Incidence of severe acute kidney failure (creatinine increase by more than 1mg/dl and/or dialysis)
- Reassessment of the primary endpoint 6 months after PCI
- Mortality within 12 months
- Cardiovascular events within 12 months (death, myocardial infarction, TLR)

## Inclusion criteria

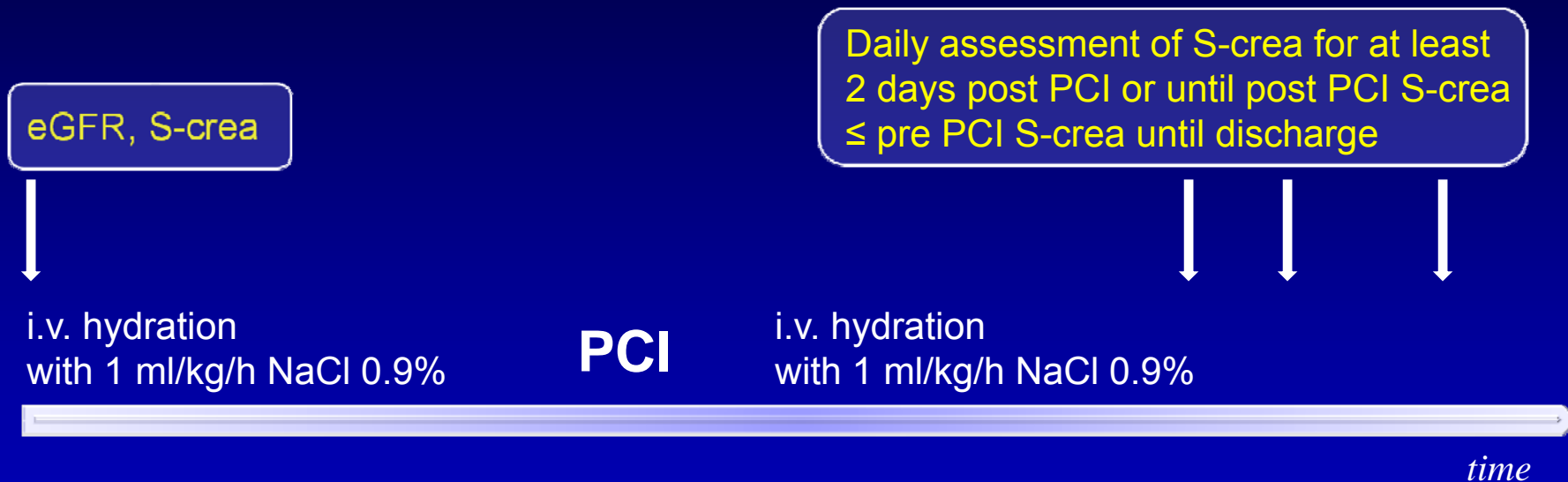
- Indication for coronary angiography with intention for PCI
- Chronic renal failure (eGFR<sup>1</sup> ≤ 60 ml/min or S-creatinine ≥ 1.5 mg/dl)
- Age ≥ 18 years, no pregnancy
- Informed, written consent

<sup>1</sup> estimated glomerular filtration rate (eGFR)  
calculated according to MDRD formula  
(Levey et al., Ann Int Med 1999)

## Exclusion criteria

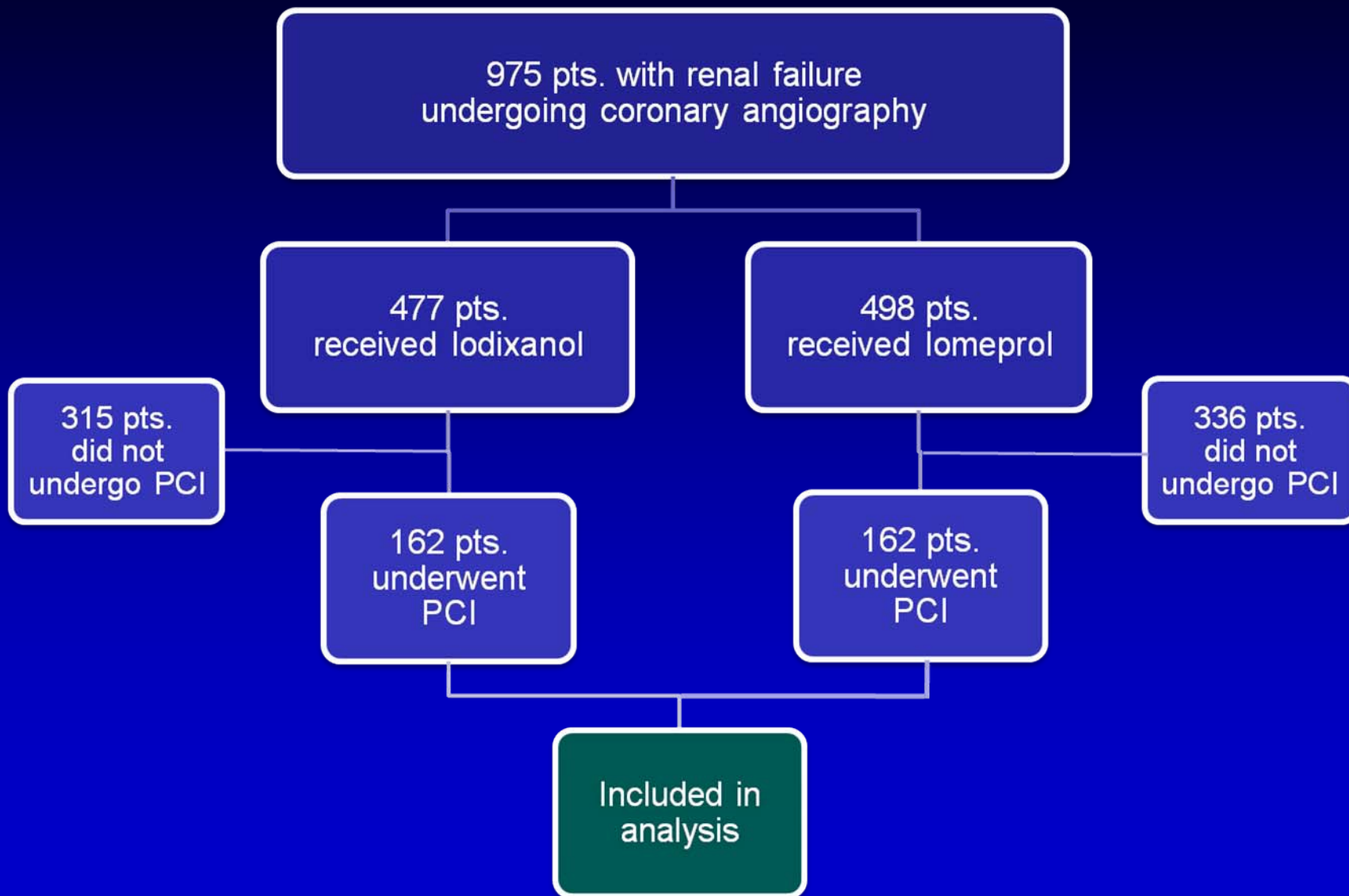
- Prior hemodialysis
- Cardiogenic shock
- Concurrent intake of nephrotoxic medication (e.g. metformin, NSAID, aminoglycosides, etc.) ≤ 48h prior contrast exposure
- Prior kidney transplantation
- Contra-indications for the use of Iodixanol or Iomeprol
- Prior or planned intravascular administration of iodine-containing contrast medium at least 7 days before or after catheterization

# Study protocol



No use of N-acetyl cysteine (NAC)

# Study flow chart



# Baseline clinical characteristics

	<b>Iodixanol 320</b>	<b>Iomeprol 350</b>	<b>P</b>
Age, years	75.0 ± 9.1	73.2 ± 9.1	.08
Male, %	73.5	71.6	.71
Diabetes, %	37.0	37.7	.91
IDDM, %	14.2	13.6	.87
History of smoking, %	37.6	30.3	.15
Hypertension, %	93.8	97.5	.10
Hypercholesterolemia, %	94.4	90.1	.15
Prev. MI, %	29.3	32.7	.55
Prev. CABG, %	25.9	19.1	.14
Ejection fraction, %	51.4 ± 12.0	49.3 ± 13.0	.28

# Baseline clinical characteristics

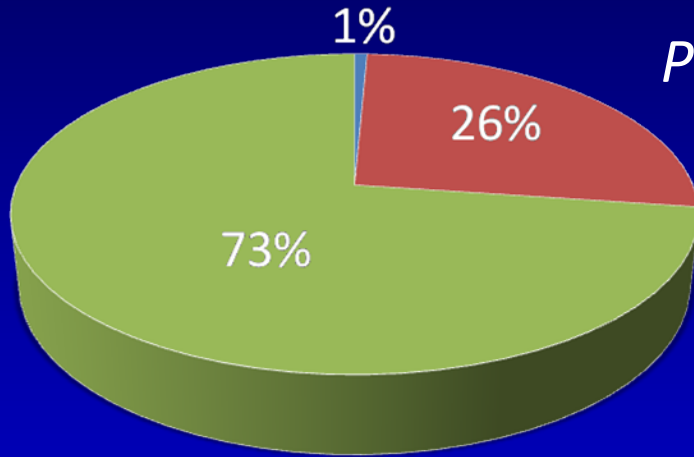
	Iodixanol 320	Iomeprol 350	<i>P</i>
STEMI, %	5.7	3.1	.27
NSTEMI ACS, %	13.6	9.9	.24
Stable Angina or silent ischemia, %	80.7	87.0	.22

	Iodixanol 320	Iomeprol 350	<i>P</i>
S-creatinine prior PCI	1.36 ± 0.51	1.37 ± 0.33	.74
S-urea prior PCI	55.6 ± 23.7	57.8 ± 27.4	.44
eGFR prior PCI	46.4 ± 9.3	47.1 ± 9.0	.44

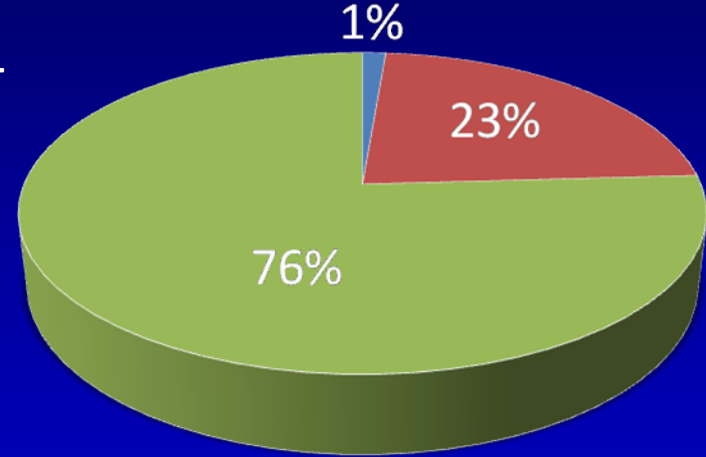
S-creatinine [mg/dl]; S-urea [mg/dl]; eGFR [ml/min/1.73m<sup>2</sup>]

# Distribution of eGFR in study population

Iodixanol



Iomeprol



$P=0.64$

■ eGFR ≤ 20 ■ 20 < eGFR ≤ 40 ■ 40 < eGFR ≤ 60

# Angiographic characteristics

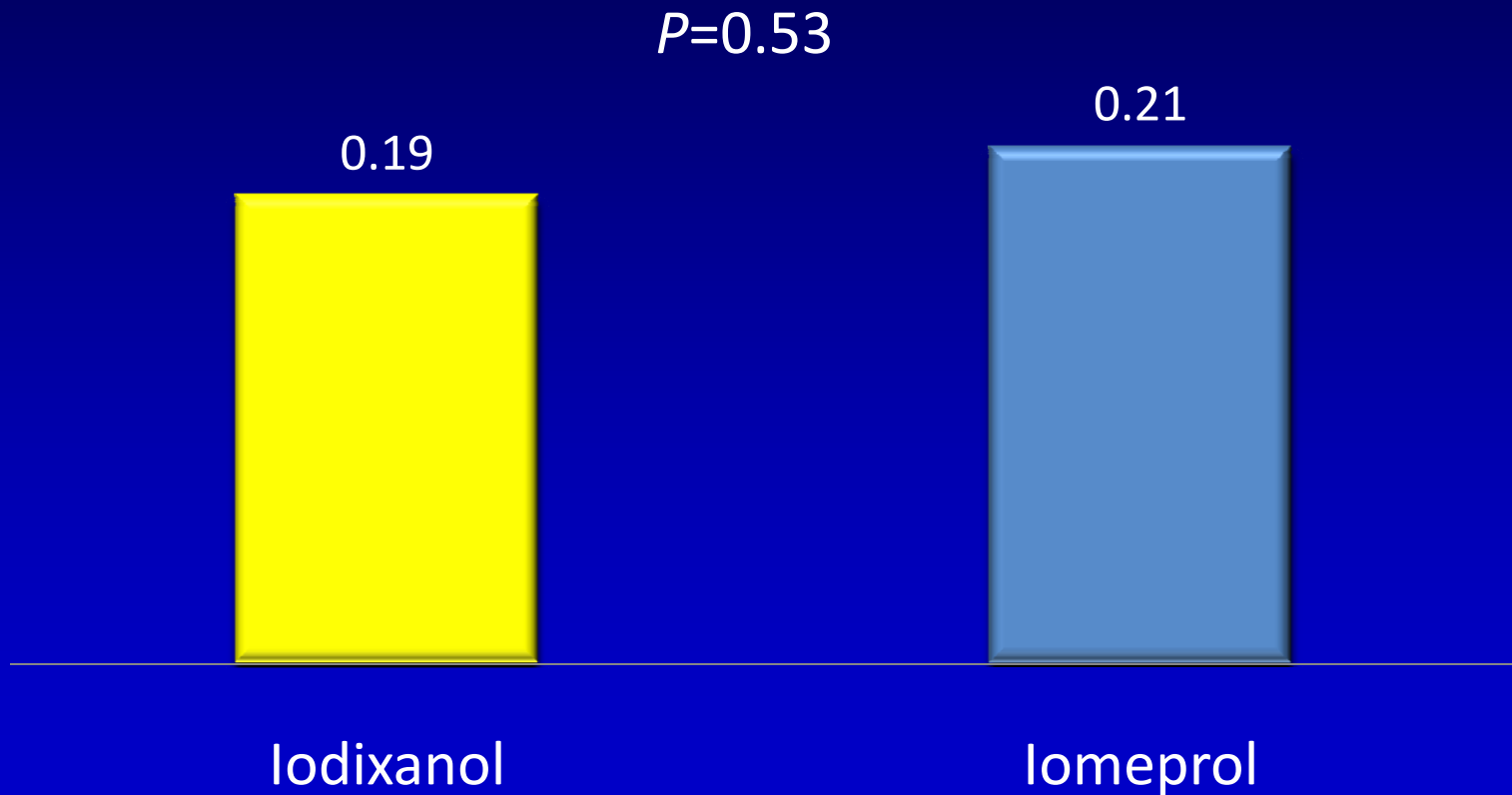
	Iodixanol 320	Iomeprol 350	<i>P</i>
Diseased vessels			.31
- 1-vessel disease, %	7	12	
- 2-vessel disease, %	22	20	
- 3-vessel disease, %	67	68	
Complex lesions (B2/C), %	78	78	.96
Number of lesions treated, n	1.7 ± 0.9	1.6 ± 0.8	.19
> 1 lesions treated, %	43	41	.65
Chronic occlusions, %	5	10	.05
Contrast volume, ml	365 ± 158	367 ± 170	.93

# Results – renal function post PCI

	Iodixanol 320	Iomeprol 350	<i>P</i>
Max. S-creatinine post PCI	1.55 ± 0.58	1.59 ± 0.48	.51
Max. S-urea post PCI	59.4 ± 30.8	61.2 ± 30.0	.59

S-creatinine [mg/dl]; S-urea [mg/dl]

Maximal rise in S-creatinine post PCI [mg/dl]



**CIN** maximal rise in S-creatinine  $\geq 0.5$  mg/dl  
or  $\geq 25\%$  of initial value

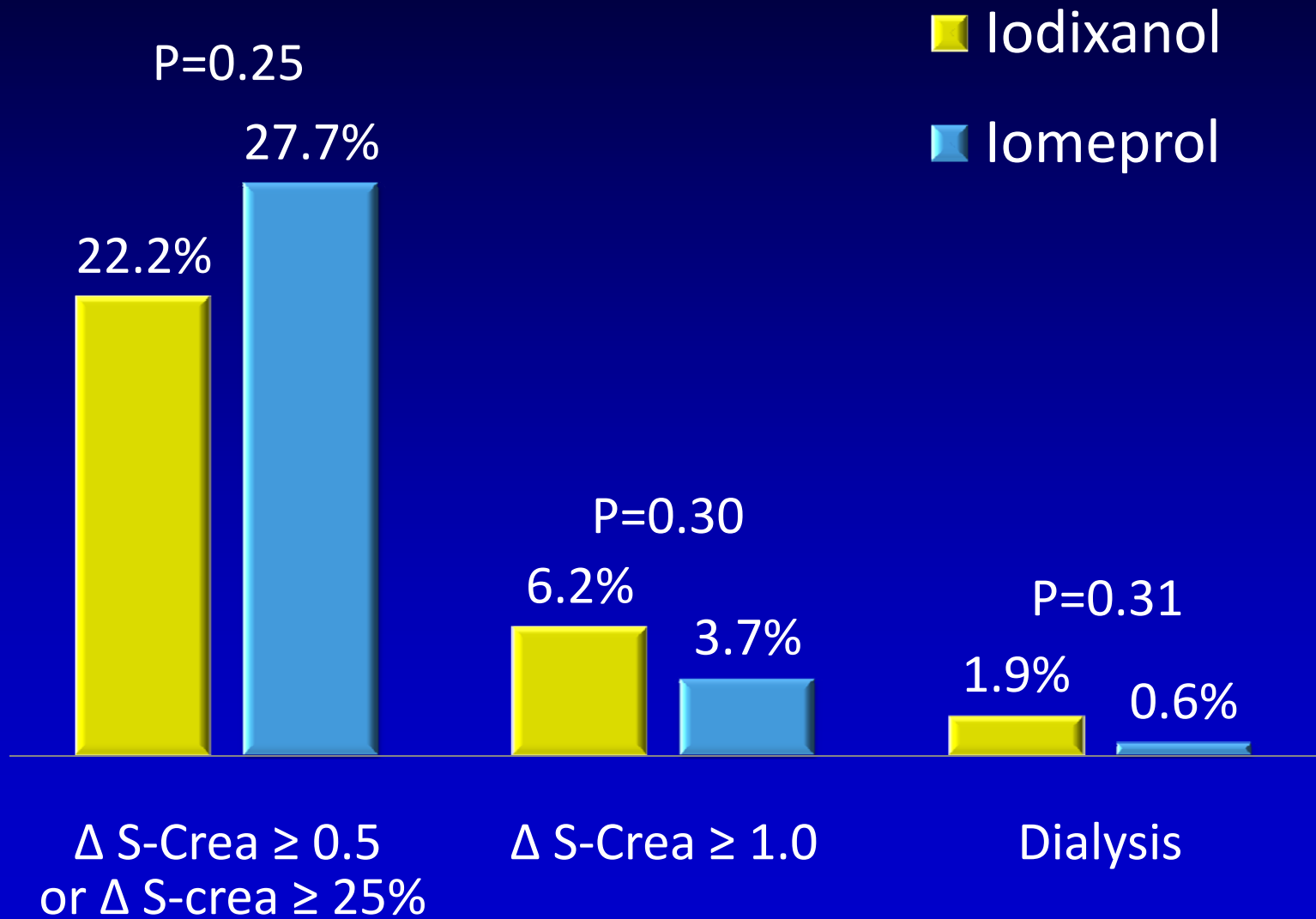
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**Severe CIN** maximal rise in S-creatinine  $\geq 1$  mg/dl

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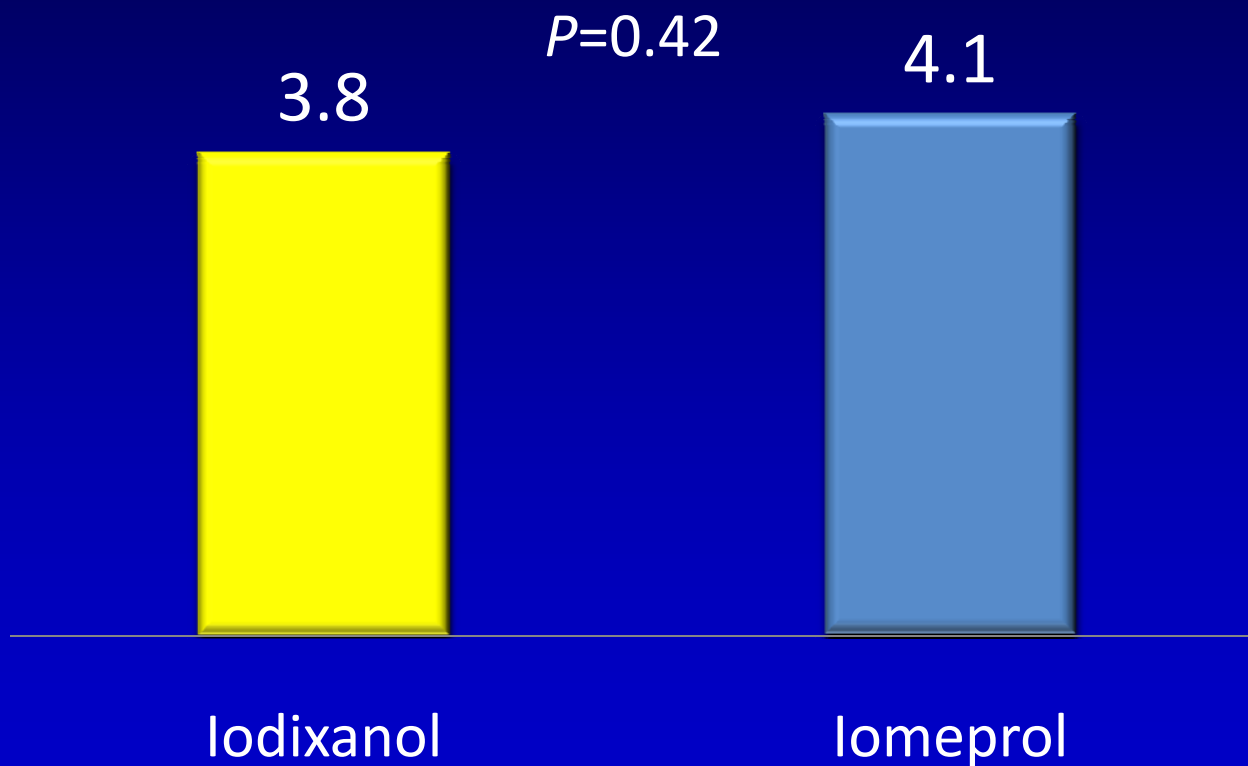
**Dialysis** hemodialysis required subsequent to  
exposure to contrast medium

# Contrast-induced nephropathy



# Hospitalization

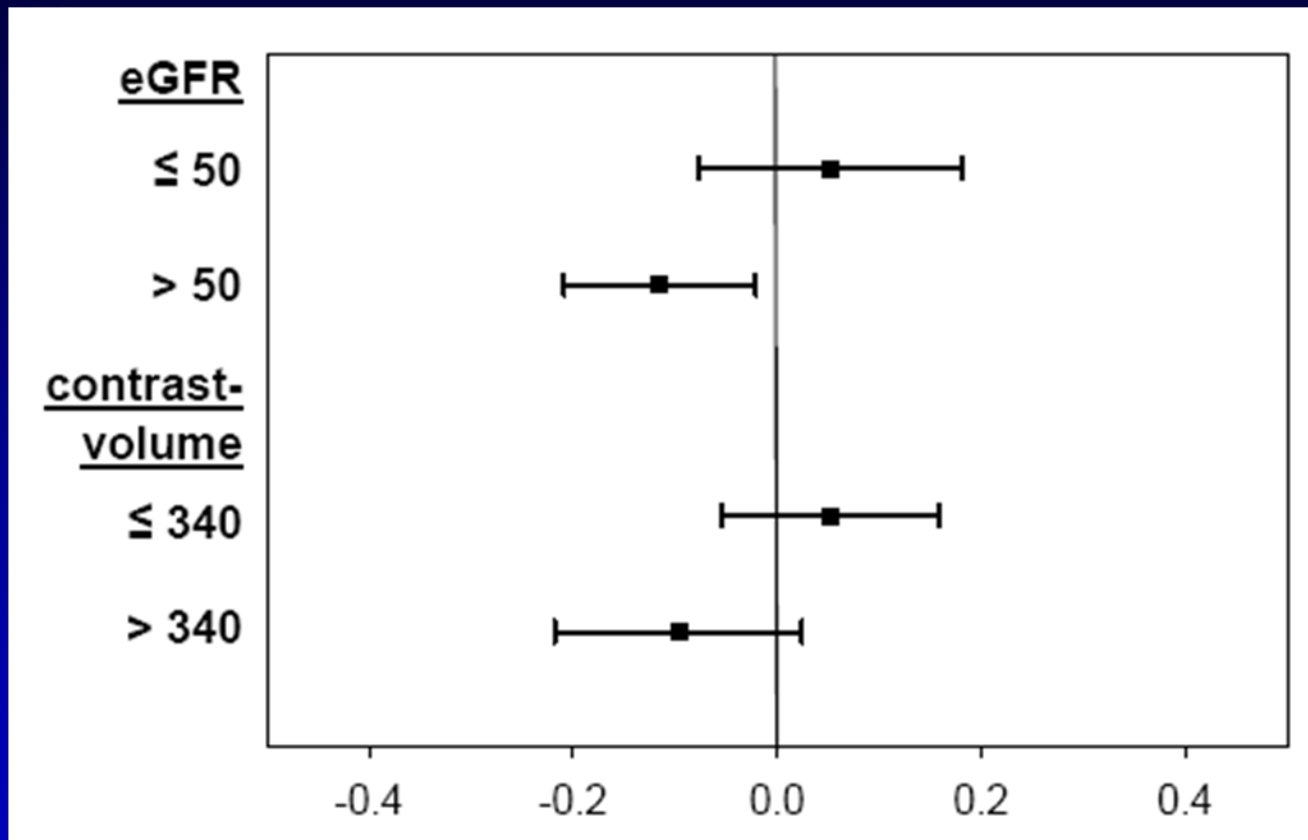
Mean duration of hospitalization subsequent to PCI [days]



# Subgroup analysis: eGFR and contrast volume

Iodixanol better

Iomeprol better



$\Delta$  S-creatinine

eGFR [ml/min/1.73m<sup>2</sup>];

contrast volume [ml];

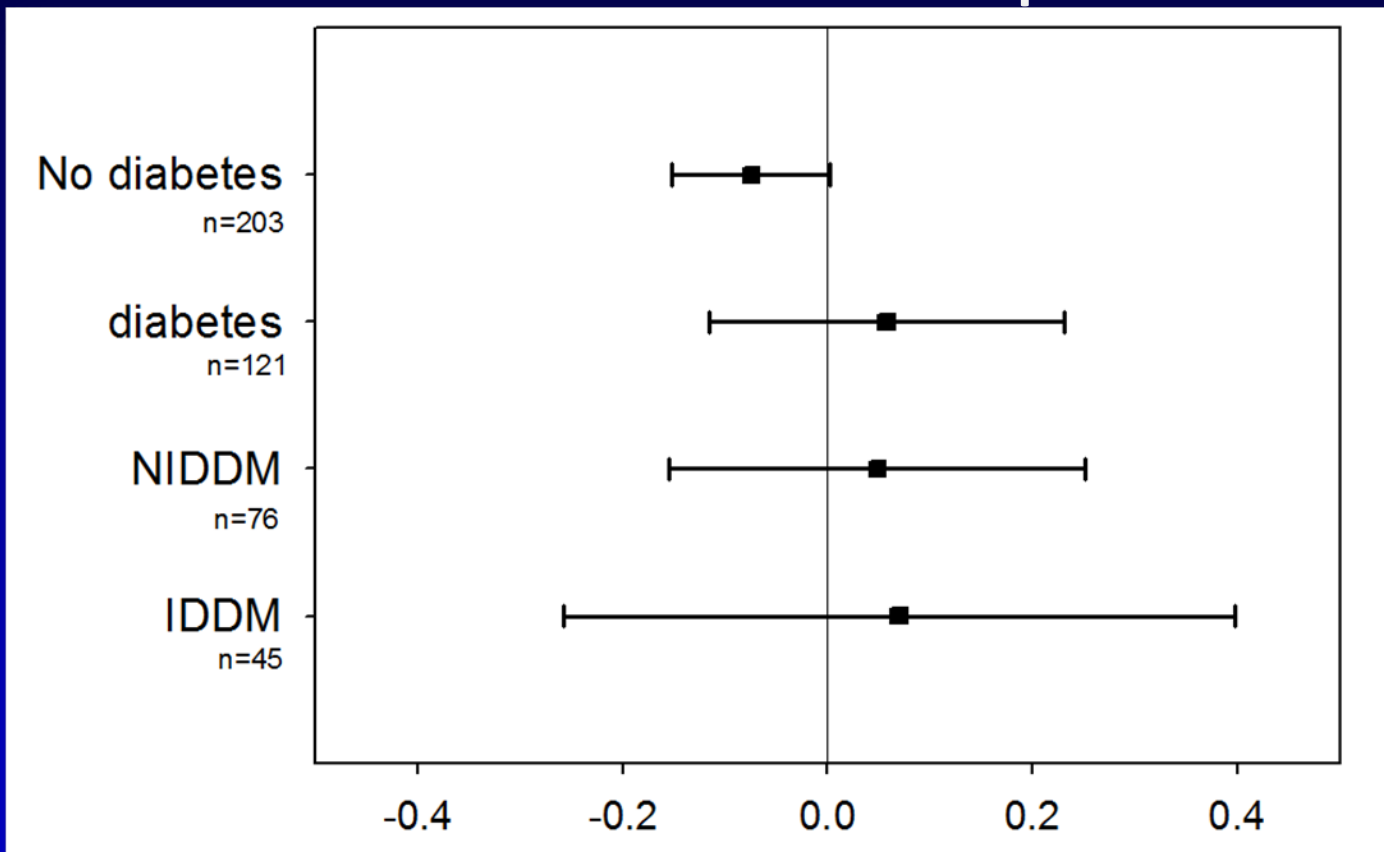
$\Delta$  S-creatinine [mg/dl];

groups were categorized according to the median value of eGFR or contrast volume in the study, respectively

# Subgroup analysis: diabetes

Iodixanol better

Iomeprol better



Δ S-creatinine

# Clinical 90-day follow up

	<b>Iodixanol 320</b>	<b>Iomeprol 350</b>	<b>P</b>
Death, %	1.2	1.8	.65
Myocardial infarction, %	3.7	4.3	.77
Target lesion revasc., %	2.5	2.5	1.00
Stent thrombosis, %	0	0	N/A
MACE, %	6.2	6.8	.82

# Conclusions

The findings of the CONTRAST study indicate that the iso-osmolar contrast medium Iodixanol induces similar nephrotoxicity compared to the low-osmolar contrast medium Iomeprol when used for PCI in patients with CRF.

Analogously, the major adverse cardiovascular event rate at 90 days is not different in the given scenario.