efficAcy and safety of Trimetazidine in Patients having been treated by Percutaneous Coronary Interventions (PCI)

Roberto Ferrari, Nicolas Danchin, Ian Ford, Kim Fox, Michal Tendera and Petr Widimsky on behalf of the ATPpci investigators

Study supported by SERVIER

ATPPCI

- Previous studies show that angina pectoris might re-occur despite successful PCI
- There are no contemporary data on prognostic benefits of anti-anginal drugs in Post-PCI patients
- ATPCI assesses the efficacy and safety of Trimetazidine added to optimal medical therapy in patients who had a recent successful PCI for stable angina or a non-ST elevated myocardial infarction (*NSTEMI*)
- ATPCI tested the value of metabolic therapy as Trimetazidine is the only anti-anginal drug devoid of haemodynamic effects improving metabolism of ischaemic myocardium

- A total of 6007 patients from 27 countries after successful PCI (*elective or urgent*) and receiving optimal medical treatment were randomised and followed for 5 years
- **Primary endpoint**: cardiac death, hospitalisation for cardiac events, recurrent/persistent angina leading to adding, switching or increasing the dose of anti-anginal therapies or to coronary angiography

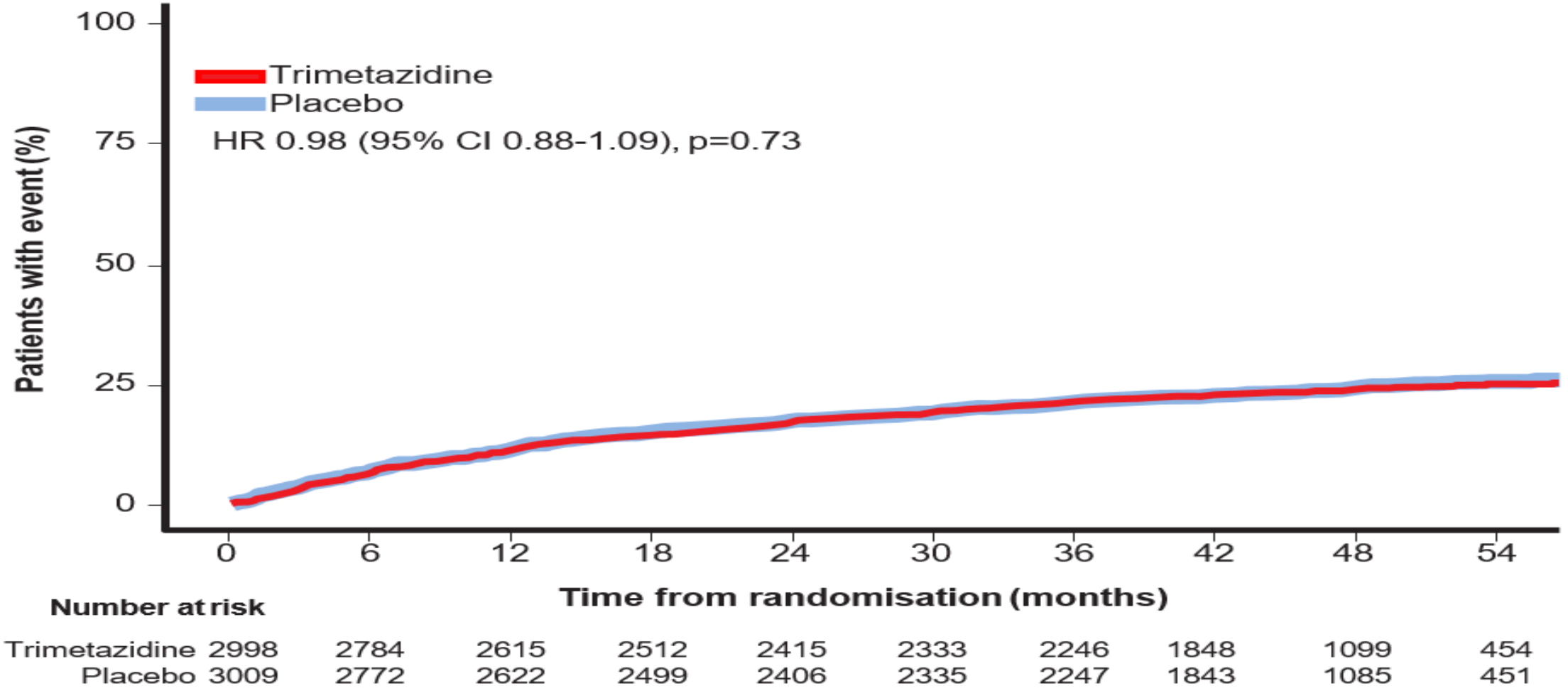
Baseline characteristics (*1*)

	Trimetazidine group (n=2998)	Placebo group (n=3009)
Age		
Mean (SD), years	61·1 (9·6)	60·7 (9·8)
≥70 years	561 (18·7%)	562 (18·7%)
<70 years	2437 (81·3%)	2447 (81·3%)
Sex		
Female	687 (22·9%)	696 (23·1%)
Male	2311 (77·1%)	2313 (76·9%)
Ethnicity		
White	2546 (84·9%)	2578 (85·7%)
Asian	241 (8·0%)	242 (8·0%)
Black	10 (<1%)	13 (<1%)
Unknown	201 (6·7%)	176 (5·8%)

Baseline characteristics (2)

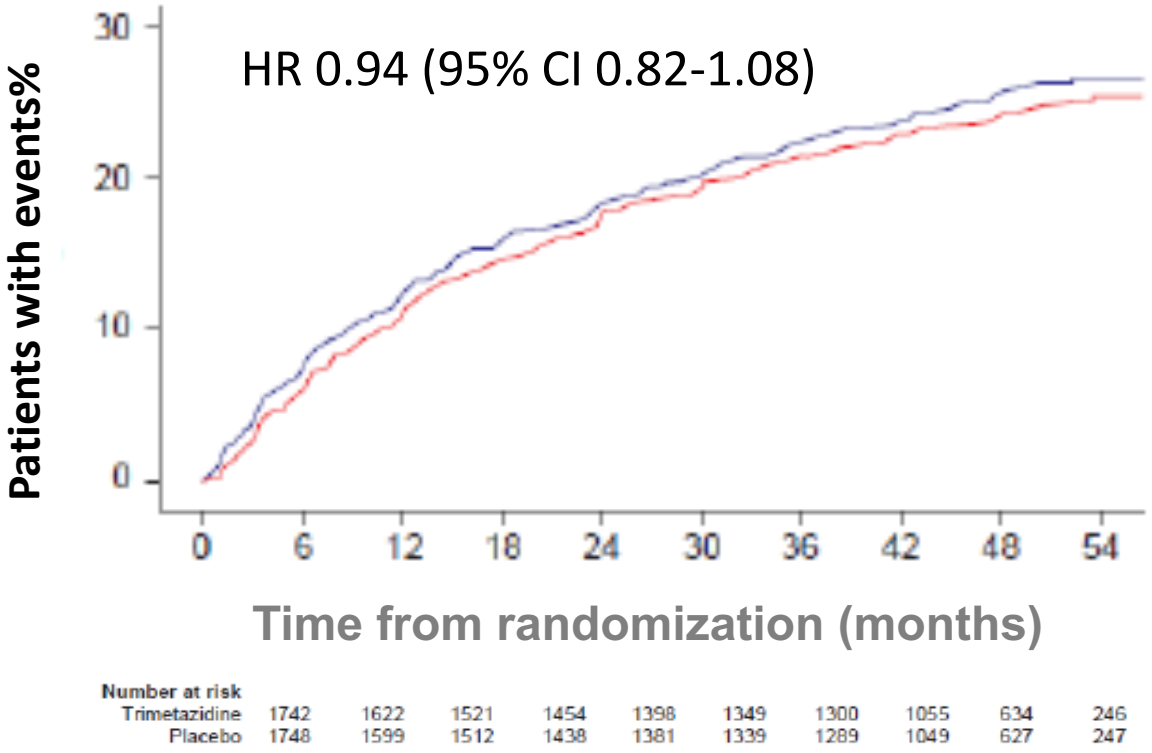
Number of stenosed vessels*		
1	1621 (54·1%)	1660 (55·2%)
2	951 (31·7%)	936 (31·1%)
3	426 (14·2%)	409 (13·6%)
Modality of revascularisation		
Urgent	1256 (41·9%)	1261 (41·9%)
Elective	1742 (58·1%)	1748 (58·1%)
Canadian Cardiovascular Society class†		
I	191 (6·4%)	240 (8·0%)
II	1223 (40·8%)	1168 (38·8%)
III and IV	1583 (52·8%)	1600 (53·2%)
Left ventricular ejection fraction‡		
<40%	54 (2·1%)	65 (2·5%)
40–49%	296 (11·3%)	307 (12·0%)
≥50%	2262 (86·6%)	2192 (85·5%)
Medical history		
Previous myocardial infarction	1448 (48·3%)	1433 (47·6%)
Previous coronary revascularisation	1002 (33·4%)	1025 (34·1%)
Hypertension	2490 (83·1%)	2482 (82 5%)
Stroke	121 (4·0%)	118 (3·9%)
Peripheral artery disease	212 (7·1%)	209 (6·9%)
Diabetes	831 (27·7%)	839 (27·9%)
Concomitant treatment ongoing at inclusion		
Antiplatelet agents	2988 (99·7%)	3004 (99·8%)
Aspirin	2930 (97·7%)	2963 (98·5%)
Clopidogrel	2402 (80·1%)	2416 (80·3%)
Ticagrelor	494 (16·5%)	484 (16·1%)
Other P2Y12 inhibitors	64 (2·1%)	77 (2·6%)
Anticoagulants	139 (4·6%)	122 (4·1%)
Lipid-lowering agents	2887 (96·3%)	2917 (96·9%)
Statins	2878 (96·0%)	2904 (96·5%)
Other	139 (4·6%)	162 (5·4%)
Angiotensin-converting enzyme inhibitors	1826 (60·9%)	1809 (60·1%)
Angiotensin receptor blockers	636 (21·2%)	655 (21·8%)
Diuretics (excluding aldosterone antagonists)	714 (23·8%)	751 (25·0%)
Antianginal therapy	2778 (92·7%)	2812 (93·5%)
β blockers	2508 (83·7%)	2530 (84·1%)
Long-acting nitrates or molsidomine	371 (12·4 %)	375 (12·5%)
Calcium channel blocker (dihydropyridine or not)	828 (27·6%)	827 (27·5%)
Other antianginal therapy§	665 (22·2%)	695 (23·1%)

Primary endpoint
Efficacy analysis set (*N=6007*)

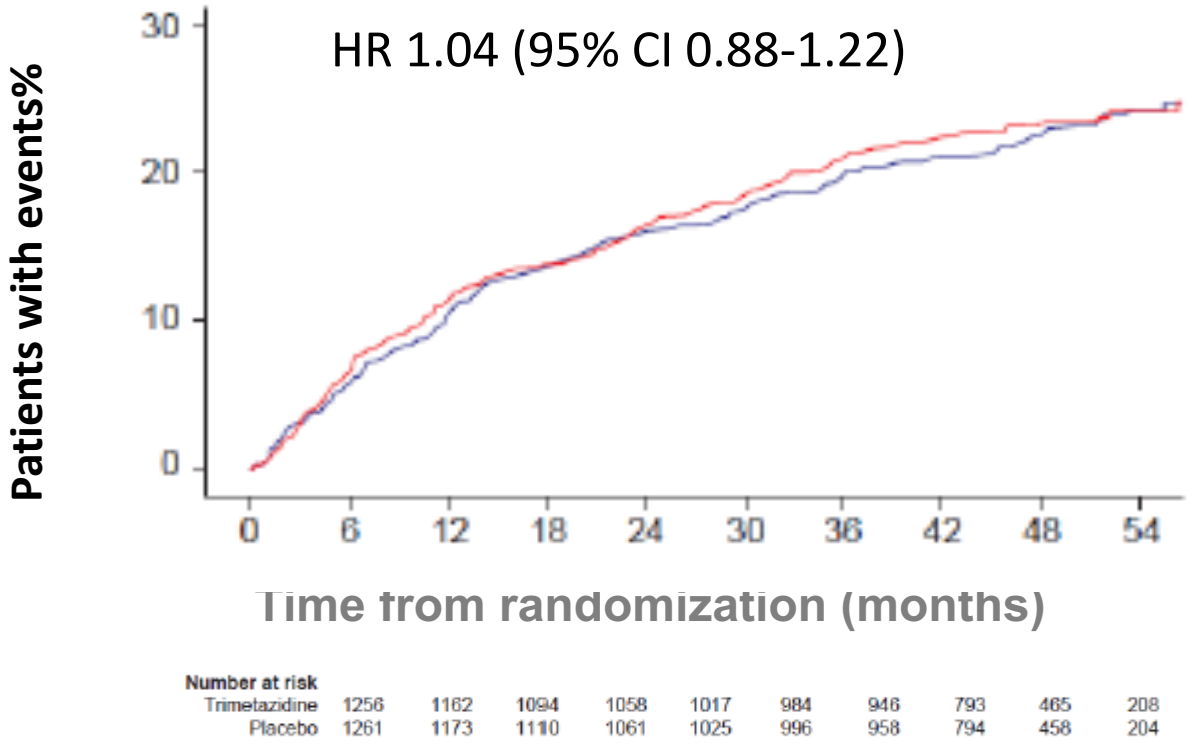


Primary endpoint: *Analysis by index PCI*
Efficacy analysis set (*N=6007*)

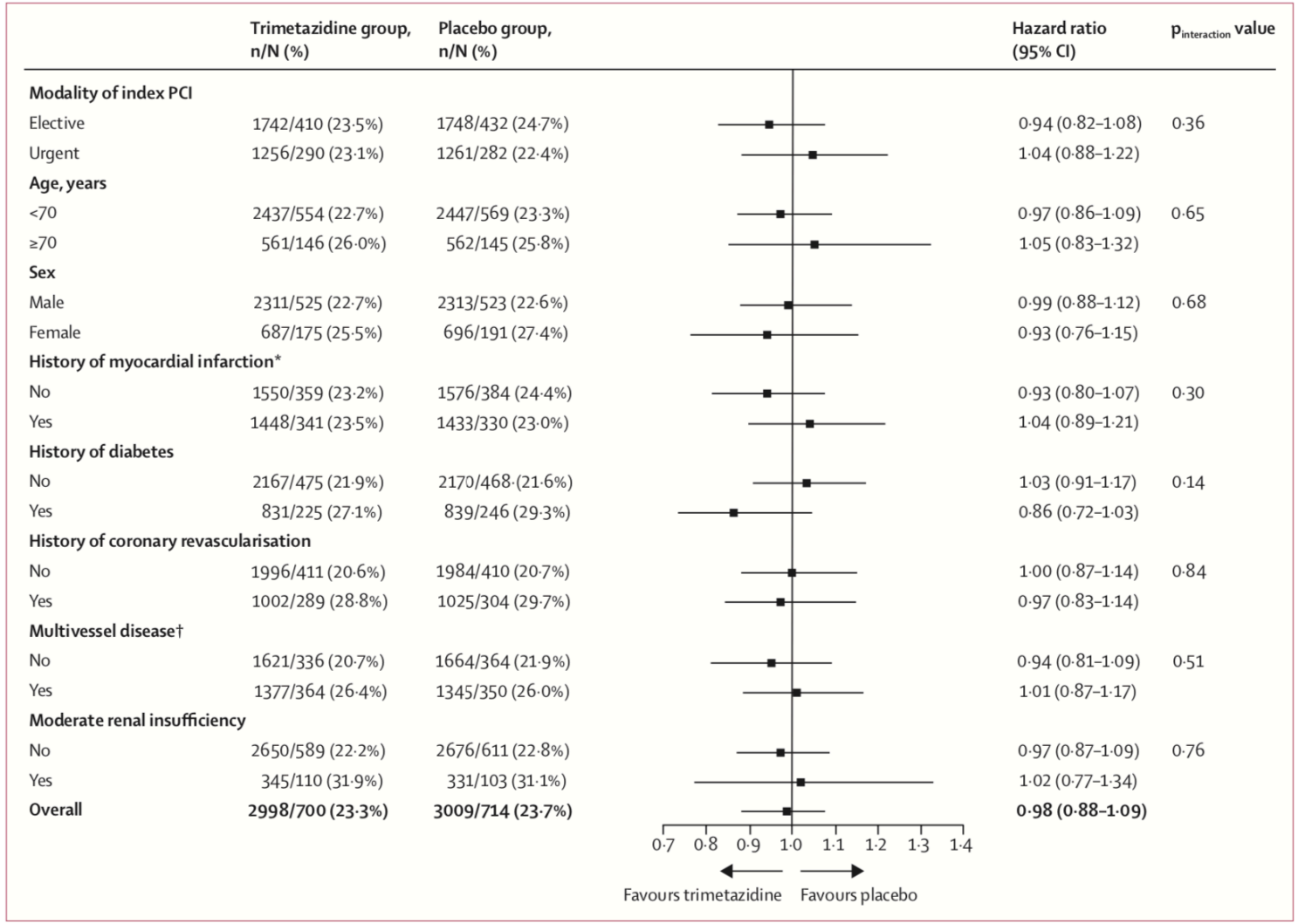
Elective PCI



Urgent PCI



	Trimetazidine group (n=2998)	Placebo group (n=3009)	Hazard ratio (95% CI)
All-cause mortality	141 (4·7%)	151 (5·0%)	0·93 (0·74–1·17)
Cardiac death or hospital admission for a cardiac event	436 (14·5%)	449 (14·9%)	0·98 (0·86–1·11)
Hospital admission for fatal or non-fatal myocardial infarction or cardiac death	176 (5·9%)	194 (6·4%)	0·91 (0·74–1·12)
Hospital admission for fatal or non-fatal myocardial infarction	129 (4·3%)	128 (4·3%)	1·02 (0·80–1·30)
Hospital admission for non-fatal myocardial infarction	122 (4·1%)	122 (4·1%)	1·01 (0·78–1·30)
Hospital admission for heart failure	66 (2·2%)	66 (2·2%)	1·01 (0·72–1·42)
Hospital admission for ischaemic chest pain	538 (17·9%)	514 (17·1%)	1·05 (0·93–1·19)
Any coronary revascularisation	357 (11·9%)	358 (11·9%)	1·00 (0·86–1·16)
Repeat coronary revascularisation in response to angina	332 (11·1%)	322 (10·7%)	1·04 (0·89–1·21)
Angina leading to coronary angiography or increase or switch in anti-anginal therapies	631 (21·0%)	624 (20·7%)	1·01 (0·91–1·13)
Ischaemia leading to coronary angiography	15 (0·5%)	18 (0·6%)	0·84 (0·43–1·67)
Ischaemia leading to an increase or switch in anti-anginal therapies	4 (0·1%)	5 (0·2%)	0·84 (0·23–3·14)



	Trimetazidine group, n/N (%)	Placebo group, n/N (%)	Hazard ratio (95% CI)	$p_{interaction}$ value
Modality of index PCI				
Elective	1742/410 (23·5%)	1748/432 (24·7%)	0·94 (0·82–1·08)	0·36
Urgent	1256/290 (23·1%)	1261/282 (22·4%)	1·04 (0·88–1·22)	
Age, years				
<70	2437/554 (22·7%)	2447/569 (23·3%)	0·97 (0·86–1·09)	0·65
≥70	561/146 (26·0%)	562/145 (25·8%)	1·05 (0·83–1·32)	
Sex				
Male	2311/525 (22·7%)	2313/523 (22·6%)	0·99 (0·88–1·12)	0·68
Female	687/175 (25·5%)	696/191 (27·4%)	0·93 (0·76–1·15)	
History of myocardial infarction*				
No	1550/359 (23·2%)	1576/384 (24·4%)	0·93 (0·80–1·07)	0·30
Yes	1448/341 (23·5%)	1433/330 (23·0%)	1·04 (0·89–1·21)	
History of diabetes				
No	2167/475 (21·9%)	2170/468·(21·6%)	1·03 (0·91–1·17)	0·14
Yes	831/225 (27·1%)	839/246 (29·3%)	0·86 (0·72–1·03)	
History of coronary revascularisation				
No	1996/411 (20·6%)	1984/410 (20·7%)	1·00 (0·87–1·14)	0·84
Yes	1002/289 (28·8%)	1025/304 (29·7%)	0·97 (0·83–1·14)	
Multivessel disease†				
No	1621/336 (20·7%)	1664/364 (21·9%)	0·94 (0·81–1·09)	0·51
Yes	1377/364 (26·4%)	1345/350 (26·0%)	1·01 (0·87–1·17)	
Moderate renal insufficiency				
No	2650/589 (22·2%)	2676/611 (22·8%)	0·97 (0·87–1·09)	0·76
Yes	345/110 (31·9%)	331/103 (31·1%)	1·02 (0·77–1·34)	
Overall	**2998/700 (23·3%)**	**3009/714 (23·7%)**	**0·98 (0·88–1·09)**	

ATPpci

- The event rate in the ATPCI population was lower than expected and required an extension of the follow-up to 5 years
- The prophylactic use of the anti-anginal-metabolic agent Trimetazidine, added to recommended medical therapy, did not improve the outcome of the ATPCI population after a successful elective or urgent PCI
- No Trimetazidine-related safety issues were identified

Take Home Messages

- Patients with stable angina and NSTEMI receiving optimised medical therapy combined with successful PCI have low events and no re-occurrence of angina
- Improvement of cardiac metabolism with Trimetazidine did not improve outcome and is not necessary
- Patients with CCS disease should:
  - Control their risk factors
  - Take the available preventive and anti-anginal drugs and, if symptoms persist, angioplasty will improve them without any re-occurrence