| Trial | COURAGE | ISCHAEMIA | FAME | FAME2 | FAME3 | DEFINE-FLAIR | ORBITA | ORBITA-2 |
|---|---|---|---|---|---|---|---|---|
| Type of study | Randomised parallel trial | Randomised parallel trial | Randomised parallel trial | Randomised parallel trial | Randomised parallel non-inferiority trial | Randomised parallel trial | Randomised control trial | Randomised control trial |
| Population | Patients with stable CAD with either stenosis >70% in ≥1 proximal epicardial coronary artery with objective evidence of myocardial ischaemia | Patients with stable CAD and moderate-severe myocardial ischaemia on non-invasive stress testing | Patients with multi-vessel CAD (stenosis >50%) in at least 2/3 major coronary arteries | Patients with one of more stenoses with ischaemia (FFR <0.8) | Patients with three vessel disease without left main involvement. | iFR vs FFR guided PCI in patients with stable angina or ACS | Patients with stable CAD with at least one severe coronary artery stenosis | Patients with stable CAD with at least one severe coronary stenosis on CTCA/invasive angiography with ischaemia on non-invasive imaging or invasive coronary physiological test. |
| Sample size | 2287 | 5179 | 1005 | 888 | 1500 | 2492 | 200 | 301 |
| Intervention | PCI with optimal medical therapy vs optimal medical therapy alone | Routine invasive therapy (angiogram and PCI or CABG as appropriate) versus medical therapy | Angiographically guided vs FFR guided PCI in patients with multi-vessel CAD | FFR guided PCI and OMT compared to OMT alone in patients with ischaemia (FFR <0.8) | FFR guided PCI with latest DES (lesions <0.80) compared to CABG with arterial graft | iFR vs FFR guided PCI | PCI with medical therapy vs sham placebo procedure with medical therapy | PCI compared to placebo procedure. Both groups off all anti-anginal medications. |
| Findings | No significant differences between groups in composite outcome of death, non-fatal MI, stroke or hospitalisation for ACS (19.5% for medical therapy vs 20% for PCI HR 1.05, 95% CI 0.87-1.27, p = 0.62) | - No significant difference in cardiovascular death, MI, resuscitated cardiac arrest or hospitalization for unstable angina or heart failure ((15.5% medical therapy vs 13.3% invasive group, p=0.34)<br>- Modest improvement in symptom benefit at 3 months amongst daily/weekly angina which persisted at 12-36 months. | No significant difference in MACE for FFR group (13.2% vs 18.3%, p = 0.02) | Significant reduction in MACE in PCI and OMT group (4.3% in PCI group vs 12.7% in OMT, HR 0.32, 95% CI 0.19-0.53, p<0.001 which was mainly driven by reduction in urgent revascularisation (1.6% vs 11.1%, p<0.001) | Higher rates of MACE at 1 year in the FFR guided PCI arm compared to CABG (10.6% vs 6.9% with HR 1.5 and CI 1.1-2.2 and p = 0.35)<br><br>No difference in MACE at the 3 years (12% vs 9.2%, CI 0.98-1.83, p = 0.07). Higher rates of MI and repeat revascularisation (7 vs 4.2%, p = 0.02 and 11.1% vs 5.9% p = 0.001 respectively) | iFR guided PCI non-inferior compared to FFR with regards to MACE (6.8% vs 7%, p<0.001) | No significant difference between groups in terms of treadmill exercise time. No change in peak oxygen uptake, exercise time to 1mm STD, angina severity (CCS class), physical limitation or angina frequency | PCI led to lower angina symptom score compared to placebo procedure |
| Limitations | - Unblinded<br>- Predominantly white (86%) men (85%).<br>- Excluded persistent class IV angina, markedly positive stress.<br>- Bare metal stents during PCIs (DES not commonplace at the time)<br>- High cross over rate >30% shifting to PCI group. | - Unblinded<br>- 34% no angina at baseline.<br>- Excluded 'unacceptable angina at baseline' | - Treating clinicians unblinded<br>- Patients recruited with lesions >50% angiographic stenosis not necessarily reflective of clinical practice<br>- Cut off of 0.8 rather than 0.75 leading to PCI of potentially functionally non-significant lesions | - Unblinded<br>- Short mandated follow up (7 months)<br>- Cross over rate of 41% from OMT to FFR guided PCI arm<br>- Trial stopped early after randomising 888 patients (original target 1623) | - 19% women, 93% white<br>- Not explicitly powered for 3-year follow up.<br>- Only 12% of patients assigned to PCI received intravascular imaging, therefore potential for further optimisation. | - | - Excluded patients with multi-vessel disease, impaired LV.<br>- 23-25% CCS 0-1 angina, low-moderate physical limitation on Seattle angina Questionnaire<br>- Short follow up (6 weeks)<br>- Small sample size (N=200) | - Short follow up (12 weeks),<br>- Small sample size (301) |