FAME 2: FFR–Guided PCI Reduces Urgent Revascularization

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Bernard De Bruyne, MD, PhD, Onze-Lieve-Vrouw Ziekenhuis, Aalst, Belgium, presented updated trial data that demonstrated that fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) reduces cardiovascular events when compared to medical therapy (MT) in patients with stable coronary artery disease (CAD).

The Fractional Flow Reserve-Guided Percutaneous Coronary Intervention Plus Optimal Medical Treatment (OMT) Versus OMT trial [FAME 2; De Bruyne B et al. *N Engl J Med*. 2014] was undertaken to determine if FFR-guided PCI improves outcomes in patients with stable CAD.

For this trial, 1220 patients with angiographically defined CAD in one or more vessels who were planned for PCI were enrolled. Patients with a history of coronary artery bypass grafting, left ejection fraction <30%, or left main CAD were excluded. Patients having at least one stenosis with FFR ≤0.80 (n=888) were randomized 1:1 to PCI with (n=447) or without (n=441) MT. The remaining 332 patients (FFR >0.80) were treated with MT and followed in a registry. Follow-up assessments were done after 1 and 6 months, and annually for 5 years. The primary end point was a 2-year composite of all-cause death, myocardial infarction (MI), or urgent revascularization. The trial was stopped after enrolling just over half of the planned patient population due to overwhelming reduction in the primary composite in patients treated with PCI. The initial results of the trial have been previously presented [De Bruyne B et al. *N Engl J Med.* 2012]. Dr De Bruyne presented updated findings that reflect the 2 years of follow-up as originally planned.

Patients in the randomized and registry groups had similar baseline demographics including prevalence of risk factors for CAD, noncardiac comorbidities, cardiac history, and prevalence of angina (Table 1).

At year 2, patients with FFR ≤0.80 who were randomized to MT had higher rates of death, MI, or urgent revascularization when compared with patients treated with PCI (HR 0.39; 95% CI, 0.26 to 0.57; *P*<.001) and patients with FFR >0.80 who were followed in the registry (HR 2.34; 95% CI, 1.35 to 4.05; *P*=.002). These outcomes were predominately driven by large reductions in urgent revascularization (HR 0.23; 95% CI, 0.14 to 0.38; *P*<.001)

Patients with FFR ≤0.80 who were randomized to PCI+MT displayed similar outcomes as patients with FFR >0.80 who were followed in the registry (HR 0.90; 95% CI, 0.49 to 1.64; *P*=.72) over the 2-year follow-up.

Table 1. FAME 2 Fractional Flow Reserve Measurements

	Randomized Trial n=888		Registry n=332	*P*[a]
Patients, n	PCI+MT=447	MT=441	With FU=166	
FFR significant stenosis (No. per patient)	1.51±0.78	1.43±0.76	0.03±0.17	<.001
No. of vessels with ≥1 significant stenosis (by FFR) (%)				
1	74	78	3	
2	23	19	0	
3	3	3	0	
Proximal or mid-LAD stenosis (%)	62	59	0	<.001
Lesions with FFR ≤0.80 (%)	76	76	2[b]	<.001
Mean FFR in stenosis with FFR ≤0.80	0.64±0.13	0.64±0.14	(NA)[b]	

[a]*P* Value compares all RCT patients in registry.

[b]Chronic occlusions in the registry patients were arbitrarily assigned an FFR value of 0.50. These patients also had another lesion >50% with an FFR >0.80.

FFR, fractional flow reserve; FU, follow-up; LAD, left anterior descending; MT, medical therapy; NA, not applicable; PCI, percutaneous coronary intervention; RCT, randomized controlled trial.

Source: De Bruyne B et al. *N Engl J Med*. 2014

A landmark analysis was also performed at day 7. Patients randomized to PCI had higher rates of death or MI at week 1 (HR 9.01; 95% CI, 1.13 to 72.0). However, in those patients who had no events in week 1, treatment with PCI reduced death or MI by 44% (HR, 0.56; 95% CI, 0.32 to 0.97).

The reduction in urgent revascularization within week 1 after randomization to PCI+MT did not achieve statistical significance when compared to MT (HR 0.49; 95% CI, 0.09 to 2.70). However, from day 8 to year 2, treatment with PCI+MT reduced urgent revascularization (HR 0.21; 95% CI, 0.12 to 0.37). After year 2, more than 40% of the MT patients required revascularization.

Although symptoms decreased in all patients beginning at day 30, the proportion of patients improved was greater in the patients treated with PCI+MT.

In conclusion, in patients with stable CAD, treatment with FFR ≤0.80 and PCI experienced resulted in >50% fewer deaths, MIs, or urgent revascularizations than treatment with MT. These findings provide strong support for the value of FFR-guided PCI in patients with stable angina.