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## **The year in review 2019: Coronary interventions**

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**Classifications:** ACS / NSTEMI-ACS; NSTEMI; STEMI; Stable angina; Clinical research; Clinical trials

## List of abbreviations

ACS: acute coronary syndrome

AF: atrial fibrillation

BMS: bare-metal stent

CAD: coronary artery disease

CCS: chronic coronary syndrome

CTO: chronic total occlusion

DAPT: dual antiplatelet therapy

DCB: drug-coated balloon

DES: drug-eluting stent

DM: diabetes mellitus

DoCE: device-oriented composite endpoint

FFR: fractional flow reserve

IVL : intravascular lithotripsy

IVUS : intravascular ultrasound

LCBI : lipid Core Burden Index

MACE : major Adverse Cardiovascular Events

MI : myocardial infarction

MRI: magnetic resonance imaging

NIRS: near-Infrared Spectroscopy

NOAC: non-Vitamin K antagonist oral anticoagulants

NSTEMI: non-ST-elevation myocardial infarction

PCI: percutaneous coronary intervention

PS: provisional stent

ST: stent thrombosis

STEMI: ST-elevation myocardial infarction

TLF: target lesion failure

TLR: target lesion revascularization

TVF: target vessel failure

## **Introduction**

Since nearly 30 years ago, the antiplatelet therapy was introduced and remains the cornerstone of Percutaneous Coronary Interventions (PCI). In the year of 2019, results of several pivotal trials seemed to herald a new era of antiplatelet therapy -the era of aspirin-free strategy. In the same year, the debates of the optimal revascularization strategy for patients with left main or multivessel disease were reignited; the attempt of early infusing alteplase after coronary reperfusion to reduce microvascular obstruction was disproven, and the result of the ISCHEMIA trial showed no advantage of routine invasive treatment in patients with chronic coronary syndrome (CCS).

New publications and research related to coronary interventional practice have emerged and will be highlighted in this review, which comprises the prominent interventional cardiology publications from the high-impact journals: New England Journal of Medicine, Lancet, JAMA (including JAMA Cardiology), European Heart Journal, Journal of the American College of Cardiology, Circulation, JACC Cardiovascular Interventions, Circulation Cardiovascular Interventions, and EuroIntervention. The focus of this article is to summarize the findings of the pivotal trials (illustrated in Figure 1) and their impact on clinical practice.

### **1. Drug-eluting stents**

There are numerous trials conducted comparing the outcomes among second-generation drug-eluting stents (DES), but few of them exhibited superiority of one over the other. In 2017, the BIOFLOW V [1] study demonstrated that the ultra-thin struts (60um) stent Orsiro was superior to Xience in terms of target lesion failure (TLF) in an all-comers population. This year, the BIOSTEMI trial [2] further demonstrated the superiority of Orsiro over Xience in STEMI patients. At 12 months, the primary endpoint of TLF occurred in 25 (4%) of 649 patients treated with Orsiro and 36 (6%) of 651 patients treated with Xience (RR 0.59, 95% Bayesian credibility interval 0.37-0.94; posterior probability of superiority 0.986). Another trial comparing the efficacy of ultra-thin struts DES is the TALENT trial [3]. In an all-comer population, the Supraflex, also a 60um ultra-thin struts stent, was non-inferior compared to Xience at 12 months in terms of Device-Oriented Composite Endpoint (DoCE), a composite endpoint of cardiac death, target-vessel myocardial infarction (MI) or clinically indicated target-lesion revascularization (TLR). The DoCE occurred in 35 (4.9%) of 720 patients in the Supraflex arm and 37 (5.3%) of 715 patients in the Xience arm ( $P_{\text{non-inferiority}} < 0.0001$ ). With aggregated results of the ultra-thin struts stents, it seems that these DES might serve as the new “standard of care” in the near future. However, we still need long-term results showing that the efficacy is preserved before we change our practice.

Other non-inferiority trials published this year, include the ReCre8 trial [4], which demonstrated that the Cre8 stent is non-inferior to Resolute Integrity; and the SORT-OUT VIII trial [5], which showed that the BioMatrix NeoFlex was non-inferior to Synergy. Both trials were performed in an all-comers population and used TLF at 12-month as the primary endpoint. The MASTER trial [6] and BIOFLOW-IV trial [7], which both used target vessel failure (TVF) rate at 12 months as primary endpoint, showed

that the Ultimaster DES was non-inferior to the Kaname bare-metal stent (BMS) for PCI treatment of STEMI patients, and Orsiro was non-inferior to Xience Prime/Xpedition, respectively. These trials are summarized in table 1.

The assessment of extended long-term outcomes for DES is limited, especially regarding the comparison among second-generation DES. This year, the 10 years result of the ISAR-TEST 4 trial [8] was published. The study showed that second-generation DES, with either a permanent (Xience) or biodegradable polymer (Yukon Choice PC), were associated with better outcomes at 10 years, as compared with an early-generation DES with a permanent polymer (Cypher). The 10-year incidence of major adverse cardiac event (MACE), which consisted of death, MI, or TLR was 47.7% in Yukon Choice PC arm, 46.0% in Xience arm, and 54.9% in Cypher arm ( $P=0.003$ ).

For DES versus BMS, the 5-year results of the COMFORTABLE AMI study [9] strengthened the more favorable earlier results of DES over BMS. In addition, two patient-level meta-analyses, one including 10,979 STEMI patients from 15 studies with a mean follow-up of 3 years [10], the other including 26,616 patients from 20 randomized trials with a mean follow-up of 3.2 years [11], both showed that the risk of the composite endpoint, cardiac death or MI was reduced in DES compared with BMS recipients.

## 2. Drug-coated balloons

The BASKET-SMALL 2 trial [12] published in 2018 has shown that in small native coronary artery disease (CAD), paclitaxel-based drug-coated balloon (DCB) was non-inferior to DES regarding TVF up to 12 months. The DEBUT trial [13] published this year, aimed to compare the efficacy of DCB with BMS among patients with *de novo* lesions (reference vessel diameter of 2.5-4.0 mm) and a high bleeding risk. After 9 months, the primary outcome (cardiovascular death, MI, TLR) occurred 1 of 102 (1%) in DCB arm and 15 of 106 (14%) in BMS arm ( $P_{\text{superiority}} = 0.00034$ ). 5 of 102 patients assigned to the DCB group received additional treatment for another lesion (3 with DES and 2 with BMS) and 23 of 106 patients in the BMS group received additional treatment for another lesion (22 with DCB and 1 with DES). There were also three lesions (2%) in two patients required bailout stenting in the DCB group. Notably, in both arms, DAPT was used for only one month in this trial.

The DEBUT trial is so far the first RCT investigating the DCB only strategy in large *de novo* coronary artery lesions, and the results indicate that the use of DCB was superior to BMS among patients undergoing *de novo* PCI with a high bleeding risk. Nevertheless, the reference device of that study, BMS, is not the optimal comparator, since the most recent European Society of Cardiology guidelines [14] recommend DES over BMS, even in high bleeding risk patients. The short duration of DAPT (three months) seem to be effective in high bleeding risk patients. Moreover, trials regarding bioabsorbable polymer DES, such as LEADERS FREE [15] have shown the safety of 1-month DAPT with those stents. Thus, the optimal control of the DEBUT study might be bioabsorbable polymer DES with shorter durations of DAPT. However, based on the low MACE rate showed in the study, DCB might be a reasonable option for the high bleeding risk patients.

Another interesting trial regarding DCB published in 2019 is the REVELATION trial [16], which aimed to compare DCB versus DES in PCI for STEMI patients. Patients with a *de novo*, non-severely calcified culprit lesion, and a residual stenosis of <50% after pre-dilatation were enrolled. The primary endpoint was the fractional flow reserve (FFR) value of the infarct-related lesion. At 9 months after enrollment, the mean FFR was  $0.92 \pm 0.05$  in the DCB group (n =35) and  $0.91 \pm 0.06$  in the DES group (n = 38) (P =0.27). There are no cardiac death or recurrent MI events in any treatment group. 2 of 58 patients (3%) in the DCB group and 1 of 54 patients (2%) in the DES group had TLR.

Although it is still too early to conclude that the use of DCB and DES have comparable clinical outcomes in treating STEMI patients, the presented results are one step forward to show the safety and feasibility of the DCB only strategy.

In-stent restenosis (ISR) represents the most common cause of treatment failure after percutaneous coronary intervention and the current practice for treating ISR are angioplasty with DCB or repeat stenting with DES. The DAEDALUS study [17] published in 2019 is a patient-level meta-analysis, which included 1976 patients from 10 RCT trials, comparing the angioplasty with DCB and repeat stenting with DES in patients undergoing treatment for ISR. The results showed that at 3-year follow-up, DCB was associated with a significant increase in the risk of TLR compared with DES [hazard ratio 1.32, 95% CI 1.02-1.70, P = 0.035]. The number-needed-to-treat was 28.5 in DES group to prevent an TLR event compared to DCB. The primary safety endpoint of all-cause death, myocardial infarction, or target lesion thrombosis was comparable between treatments (HR 0.80, 95% CI 0.58–1.09, P = 0.152).

### 3. Revascularization strategy

#### Left main and multivessel disease

The long-term results of several landmark trials comparing the revascularization strategy of PCI versus CABG were reported in 2019 (summarized in Figure 2).

The SYNTAX Extended Survival Trial (SYNTAXES) [18] reported the 10-year results of the SYNTAX trial, in which investigators randomized 1,800 patients with *de-novo* three-vessel or left main CAD to receive PCI or CABG during 2005-2007. At 10 years, 244 (27%) of 841 patients died after PCI and 211 (24%) of 848 died after CABG ( $P_{\text{superiority}}=0.092$ ). Among patients with three-vessel disease, 151 (28%) of 546 patients died after PCI; 113 (21%) of 549 died after CABG (HR 1.41 [95% CI 1.10–1.80]), and among patients with left main CAD, 93 (26%) of 357 died after PCI versus 98 (28%) of 348 died after CABG (0.90 [0.68–1.20];  $P_{\text{interaction}}$  for 3VD vs LM =0.019). Patients with the higher SYNTAX score ( $\geq 33$ ) benefited more from CABG than from PCI, whereas patients with lower or intermediate scores had similar results with either revascularization strategy.

The FREEDOM Follow-On study [19] showed the 7 years results of the FREEDOM trial [20], which compared the outcomes of PCI with CABG in patients with Diabetes Mellitus (DM) and

multivessel coronary disease. The results showed that the all-cause mortality rate was significantly higher in the PCI group than in the CABG group (24.3% [159 deaths] vs. 18.3% [112 deaths],  $P_{\text{superiority}} < 0.01$ ). Another finding was that younger patients benefit more from CABG than older patients. For patients who were 63.3 years or younger, all-cause mortality at 7.5 years was 10.2% with CABG surgery and 20.7% with PCI. Comparatively, for those who were 63.3 years or older, the rate of all-cause mortality was 27.6% with CABG and 26.3% with PCI ( $P = 0.01$  for interaction by age). These long-term follow-up results supported the revascularization strategy of CABG in diabetic patients with multivessel CAD, regardless of SYNTAX score.

The most contested result this year is the 5-years result of the EXCEL trial. The trial enrolled patients with left main CAD of low or intermediate anatomical SYNTAX score ( $\leq 32$ ) to undergo PCI or CABG. At 5 years, the primary endpoint (all-cause death, stroke, or MI) occurred in 22.0% of the patients in the PCI group and 19.2% of the patients in the CABG group ( $P_{\text{superiority}} = 0.13$ ). However, the secondary endpoint, death from any cause occurred more frequently in the PCI group than in the CABG group (13.0% vs. 9.9%; difference, 3.1%; 95% CI, 0.2 to 6.1). Based on the primary findings, the authors concluded that in patients with left main CAD of low or intermediate anatomical complexity, there was no significant difference between the outcomes of PCI and CABG with respect to the rate of a composite outcome of all-cause death, stroke, or MI at 5 years. However, such conclusion has raised heated debates, such as whether the peri-procedural MI's should be included and contribute to the composite primary endpoint -EXCEL trial included peri-procedural MI's, whereas the NOBLE trial [21] did not. The NOBLE trial, which enrolled patients regardless of their SYNTAX score, showed that CABG outperformed PCI in treating patients with left main stem CAD. The contests of the optimal revascularization strategy for these patients will last. For now, in light of EXCEL and NOBLE, a more cautious recommendation for PCI should be adopted in this setting.

### **OMT versus PCI in stable CAD patients**

One of the greatest highlights of the year in the field of coronary intervention, or at least the one that gained the greatest attention, was the presentation of the ISCHEMIA trial. Ever since the controversial results of the COURAGE [22] and the ORBITA trial [23], practitioners have been hoping for more conclusive and contemporary results from the large ISCHEMIA trial (<https://www.ischemiatrial.org>) [24]. In this study, investigators randomized 5,179 patients with stable CAD and moderate to severe myocardial ischemia on noninvasive stress testing, to test whether routine invasive therapy was associated with a reduction in ischemic events compared with optimal medical therapy (OMT). Results showed that at 3.3 years, the primary outcome (cardiovascular death, MI, resuscitated cardiac arrest, or hospitalization for unstable angina or heart failure) occurred in 13.3% of the routine invasive group compared with 15.5% of the OMT group ( $P_{\text{superiority}} = 0.34$ ). Invasive therapy was associated with harm (2% absolute increase) within the first 6 months and benefit within 4 years (2% absolute decrease). The rate of all-cause death was 6.4% in the routine invasive group as compared with 6.5% in the OMT group ( $P_{\text{superiority}} = 0.67$ ). Regarding the quality of life after PCI,

improvement in symptoms was observed among those with daily/weekly/monthly angina, but not in those without angina.

The result of the ISCHEMIA trial showing that the revascularization does not lower rates of death, heart failure, or cardiac arrest in the enrolled patients was not astonishing, since previous studies have indicated that PCI offered little advantage over OMT for these endpoints. However, the study demonstrated that early intervention is safe for patients who prefer to minimize the burden of medical therapies, for those who have limited tolerance to medications, or for those who have persistent symptoms despite medical therapy. This study also helps interventional cardiologists in providing more accurate information to patients regarding the benefits of PCI and once again underscores the importance of shared medical decision making between physicians and patients [25]. It is noteworthy that this study did not include patients with left main stenosis, left ventricular ejection fraction <35%, accelerating anginal symptoms, or an acute coronary syndrome. For those high-risk patients, intervention with OMT remains the recommended course of treatment.

### **MRI versus FFR in planning of revascularization**

Myocardial-perfusion cardiovascular MRI is a noninvasive test for the detection of CAD that has a high concordance with FFR for ischemia detection [26], and can be used to guide revascularization. The MR-INFORM study [27] investigated in CCS patients, whether a MRI-guided revascularization is non-inferior to an FFR-based strategy. Patients with either  $\geq 2$  risk factors (smoking, diabetes, hypertension, hyperlipidemia, positive family history) or positive exercise treadmill test were included in the trial. Revascularization was recommended for patients in the cardiovascular-MRI group with ischemia in at least 6% of the myocardium or the FFR group with an FFR of 0.8 or less. The primary outcome occurred in 15 of 421 patients (3.6%) in the MRI group and 16 of 430 patients (3.7%) in the FFR group (risk difference, -0.2 percentage points; 95% confidence interval, -2.7 to 2.4), findings that met the noninferiority threshold. The percentage of patients free from angina at 12 months also did not differ significantly between the two groups (49.2% in the cardiovascular-MRI group and 43.8% in the FFR group,  $P_{\text{superiority}} = 0.21$ ). The MR-INFORM is the first trial to show that MR-perfusion imaging could guide patient management in a high-risk population with the same effectiveness as invasive angiography with FFR. To a broader aspect, it is unclear and appealing to know if other functional imaging, such as Single Photon Emission Computed Tomography or dobutamine stress, or even Computed Tomography combined with FFR would have provided similar results, since patients with angina are likely to undergo one of these tests in routine clinical practice before being referred for invasive angiography. Further, the cost-effectiveness of this strategy also needs to be investigated.

### **Complete or culprit-only revascularization strategy in acute coronary syndromes**

For ACS patients with multivessel disease, would a complete revascularization strategy be superior to a culprit-only strategy? The debate has leaned toward the affirmative in recent analyses, with the caveats that most studies in this field have been small or retrospective. Another question is whether non-culprit lesions need to be treated immediately or the operators can wait and revascularized



them in a staged procedure. The COMPLETE trial [28] aimed to unravel these puzzling questions. Investigators randomized 4,041 STEMI patients with multivessel CAD who had successful culprit-lesion PCI, to either undergo further complete revascularization or be managed on medical therapy alone. All patients had non-culprit lesions with at least 70% diameter stenosis or an FFR measurement of 0.80 or less, and the timing of complete PCI was left to operator discretion. At 3 years, rates of cardiovascular death (CD) or new MI occurred in 158 of the 2016 patients (7.8%, CD:2.9%; MI:5.4%) in the complete-revascularization group as compared with 213 of the 2025 patients (10.5% CD:3.2%; MI:7.9%) in the culprit-lesion-only PCI group ( $P_{\text{superiority}}=0.004$ ). Additionally, the benefit of complete revascularization was consistently observed regardless of the intended timing of non-culprit-lesion PCI ( $P_{\text{interaction}}=0.62$ ). The Optical Coherence Tomography substudy revealed a large proportion of thin-cap fibroatheroma in the non-culprit lesions. This may help to explain the benefit observed from multivessel revascularization.

#### 4. Bifurcation lesion

Conceptually, there is a tenet among interventional cardiologists that “the simpler the better”, i.e., the provisional stent (PS) technique is preferred over the two-stent technique whenever possible [29]. However, the results of the DKCRUSH-V study has reignited the debate in 2017 [30] indicating that in true distal left main bifurcation lesions (Medina 1,1,1 or 0,1,1), a planned DK crush 2-stent strategy resulted in a lower rate of TLF at 1-year than a PS strategy. In 2019, the conclusion is further supported by its 3-year results [31]. At 3 years, among the enrolled 482 patients, TLF occurred in 41 (16.9%) patients in the PS group and in 20 (8.3%) patients in the DK group ( $P_{\text{superiority}}=0.005$ ), mainly driven by increased target vessel MI (5.8% vs. 1.7%;  $P_{\text{superiority}}=0.017$ ) and TLR (10.3% vs. 5.0%;  $p=0.029$ ). Definite or probable ST rate at 3 years was 4.1% in the PS group and 0.4% in the DK group ( $P_{\text{superiority}}=0.006$ ). It is noteworthy that these results should be interpreted cautiously since the sample size was small and the selection of bifurcation Medina 1,1,1 could have affected the result towards a two-stent technique. Additional confirmatory studies by other investigators, such as the ongoing EBC MAIN trial (NCT02497014), will further enhance the evidences in this area.

#### Revascularization of CTO lesions

Procedural results of chronic total occlusions (CTO) PCI have improved in recent years, and PCI strategies have moved toward complete revascularization with more liberal use of CTO PCI. However, evidence in evaluating the efficacy of CTO PCI is still limited. The DECISION-CTO [32] trial is one landmark trial in the field, and showed that there was no significant difference between the CTO-PCI and the OMT strategies regarding the incidence of the composite endpoint of death, MI, stroke, or any revascularization (22.3% [n=93] versus 22.4% [n=89],  $P_{\text{superiority}}=0.86$ ), indicating that the routine CTO-PCI + OMT is not superior to OMT alone in reducing cardiovascular outcomes among patients with at least one CTO. The main limitation of the study is the high rate of crossover; 78 (19.6%) patients crossed over to receive staged CTO-PCI within 3 days of randomization. Nevertheless, DECISION-CTO is one of the first trials to compare the two therapies in a systematic fashion. CTO lesions are often referred to as the “final frontier” of PCI, but should we put our efforts to revascularize all CTO lesions?

So far, we believe the answer is still inconclusive. Further analyses will be vital to see if there are certain scenarios, such as high ischemic burden, where CTO-PCI might be beneficial compared with OMT.

## 5. Antithrombotic therapies and PCI

### The twilight of Aspirin?

Starting from 2013, a new series of studies have started to investigate the “short DAPT/aspirin-free” antiplatelet strategies [33]. Following the GLOBAL LEADERS published last year [34, 35], several additional studies of short DAPT/aspirin-free strategies were published, with more positive findings (Figure 3).

The STOP-DAPT2 trial [36] randomized 3,045 Japanese patients to receive either one month of DAPT followed by clopidogrel monotherapy or a 12 months of DAPT with aspirin and clopidogrel regimen. Results showed that at 12 months, the primary endpoint (cardiovascular death, MI, stroke, definite ST, or major or minor bleeding) occurred in 2.36% patients with 1-month DAPT group and 3.70% with 12-month DAPT group, meeting the criteria for superiority ( $P=0.04$ ). The TIMI major or minor bleeding occurred in 0.41% participants with a 1-month DAPT and 1.54% with a 12-month DAPT ( $P_{\text{superiority}}=0.004$ ).

In line with the STOP-DAPT2 trial, the simultaneously published SMART-CHOICE trial, which randomized 2,993 Korean patients to either receive a P2Y<sub>12</sub> inhibitor monotherapy after 3 months DAPT or a 12 months of DAPT, showed that the primary endpoint (all-cause death, MI, or stroke) occurred in 42 patients in the P2Y<sub>12</sub> inhibitor monotherapy group and 36 patients in the DAPT group (2.9% vs. 2.5%;  $P_{\text{noninferiority}}=0.007$ ). The rate of Bleeding Academic Research Consortium type 2 to 5 bleeding was significantly lower in the P2Y<sub>12</sub> inhibitor monotherapy group than in the DAPT group (2.0% vs. 3.4%;  $P_{\text{superiority}}=0.02$ ).

Moving forward, the TWILIGHT trial, which randomized 7,119 patients, compared ticagrelor monotherapy (3-month DAPT + 12-month ticagrelor monotherapy), with the ticagrelor plus aspirin group (15-month DAPT), the former resulted in significantly higher incidence of the primary endpoint, Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding events (4.0% vs. 7.1%,  $P_{\text{superiority}}<0.001$ ). Regarding the incidence of ischemic endpoint (composite endpoint of death, nonfatal MI, or nonfatal stroke), both groups reached noninferiority (3.9 vs. 3.9%,  $P_{\text{non-inferiority}}<0.001$ ). It is noteworthy that the TWILIGHT trial enrolled the high-ischemic risk patients; e.g., age of at least 65 years, female sex, troponin-positive ACS, DM, chronic kidney disease, multivessel CAD, bifurcation lesion treated with two stents, etc. The exciting findings of these 3 trials are that the long-term DAPT may not be necessary after PCI with contemporary stents and that dropping aspirin may be a better approach than discontinuing the P2Y<sub>12</sub> antiplatelet agent. The results were also supported by the subgroup analyses of the GLOBAL LEADERS trial, indicating that in patients with multivessel PCI [37], complex PCI [38], with long stent implantation [39] or bifurcation PCI [40], age older than 75 [41], prolonged ticagrelor monotherapy for 23-month after 1-month DAPT is associated with fewer ischemic

events (all-cause mortality and new Q-wave MI) without increasing the major bleeding events (BARC type 3 or 5), compared with standard 12-month DAPT.

### **Anticoagulant and Antiplatelet therapy in patients with atrial fibrillation and CAD**

Previous PIONEER AF-PCI [42] and RE-DUAL PCI trial [43] both showed that in patients with atrial fibrillation (AF) and required antiplatelet treatment, a new oral anticoagulant (NOAC) plus clopidogrel regimen was associated with a lower incidence of bleeding events as compared with a warfarin-based triple-antithrombotic strategy. Therefore, the current expert opinions and consensus of North American Societies recommend a NOAC plus a P2Y<sub>12</sub> inhibitor in patients with AF and ACS treated by PCI [44]. However, the European guidance, still recommends triple antithrombotic therapy in these patients [45]. This year, the ENTRUST-AF PCI, AUGUSTUS and AFIRE trial brought us more evidence regarding the optimal antiplatelet therapy for AF patients.

The ENTRUST-AF PCI [46] trial enrolled 1506 patients with AF and had a successful PCI for stable CAD or ACS to receive either edoxaban (60 mg once daily) plus a P2Y<sub>12</sub> inhibitor or a vitamin K antagonist (VKA) in combination with a P2Y<sub>12</sub> inhibitor and aspirin. The primary endpoint, 12 months major or clinically relevant non-major bleeding events occurred in 128 (17%) of 751 patients with the edoxaban regimen and 152 (20%) of 755 patients with the VKA regimen ( $P_{\text{noninferiority}}=0.001$ ).

The AUGUSTUS trial [47] is a two-by-two factorial design trial. The investigators assigned 4,614 patients with AF (who had an ACS or needed to take P2Y<sub>12</sub> inhibitor) to receive apixaban or a vitamin K antagonist (1<sup>st</sup> factorial) and to receive aspirin or matching placebo (2<sup>nd</sup> factorial). Results after 6 months follow-up showed that major or clinically relevant nonmajor bleeding was noted in 10.5% of the patients receiving apixaban, as compared with 14.7% of those receiving a vitamin K antagonist ( $P_{\text{superiority}} < 0.001$ ), and in 16.1% of the patients receiving aspirin, as compared with 9.0% of those receiving placebo ( $P_{\text{superiority}} < 0.001$ ). Patients in the aspirin group (26.2%) and the placebo group (24.7%) had a similar incidence of death or hospitalization. Based on totality of the previous and present evidence, NOAC plus a P2Y<sub>12</sub> inhibitor might be considered as the new standard of care for AF patients presented with ACS, who were previously prescribed triple antithrombotic therapy [48].

While AUGUSTUS and other pivotal trials mainly focused on the antithrombotic treatment of AF patients with ACS, the AFIRE trial studied the antithrombotic strategy in patients with AF and CCS. The AFIRE trial [49] enrolled 2,236 patients with AF who had undergone PCI or CABG more than 1 year earlier, or had stable CAD. These patients were randomly assigned to receive either rivaroxaban monotherapy (15mg) or rivaroxaban (15mg) plus a platelet inhibitor (approximately 25% of the patients received clopidogrel). The rate of the primary endpoint (death, stroke, systemic embolism, MI, or unstable angina requiring revascularization) was 4.14% in the monotherapy group and 5.75% in the combination therapy group ( $P_{\text{noninferiority}} < 0.001$ ). Monotherapy was also found superior to combination therapy for major bleeding, according to the criteria of the International Society on Thrombosis and Hemostasis, with rates of 1.62% and 2.76%, respectively ( $P_{\text{superiority}} = 0.01$ ). The current guidelines recommend mono-antiplatelet therapy with a NOAC for the type of population recruited in the AFIRE

trial [50]. However, this approach was not supported by evidence from randomized, controlled trials. The AFIRE trial now added an element for future guidelines, namely that rivaroxaban monotherapy without antiplatelet therapy might be a better approach in patients with AF and CCS.

### **Ticagrelor, prasugrel, and clopidogrel**

The ISAR-REACT 5 [51] is the first head-to-head trial comparing ticagrelor and prasugrel in ACS patients. At one year, the primary endpoint (death, MI, or stroke) occurred in 184 (9.3%) of the 2,012 patients in the ticagrelor group and 137 (6.9%) of the 2,006 patients in the prasugrel group ( $P_{\text{superiority}}=0.006$ ). Bleeding Academic Research Consortium defined type 3, 4 or 5 bleeding was observed in 5.4% of patients in the ticagrelor group, and 4.8% of patients in the prasugrel group ( $P_{\text{superiority}}=0.46$ ). The benefit of prasugrel in reducing ischemic events was not penalized by a trade-off of increased bleeding events, which were numerically higher among ticagrelor-treated patients.

It is noteworthy that the delivery strategies between the two-treatment regimen were different. For STEMI patients, both study drugs were initiated at the time of randomization, whereas in patients with unstable angina and NSTEMI, ticagrelor was given as a loading dose at the time of randomization and prasugrel was given at the time of angiography, with both arms receiving maintenance doses following PCI. Therefore, in addition to compare the two drugs, this trial was also comparing two strategies among the NSTEMI patients, namely pretreatment with ticagrelor and delayed treatment with prasugrel. Although there are some concerns regarding the trial, including the open-label design, the lack of tight oversight for drug adherence and discontinuation, and the different drug delivery strategies, the ISAR-REACT 5 is a landmark study and will have impact on our practice and future guidelines.

Current guidelines [14] favor the more potent platelet inhibitors ticagrelor and prasugrel over clopidogrel because these drugs are more effective for the prevention of thrombotic events. However, this greater efficacy comes with a higher risk of bleeding. Reports suggested that approximately 30% of Caucasian patients have an inadequate response to clopidogrel as measured with platelet-function tests, and the variation in response can be partially explained by genetic variations. In patients without these loss-of-function alleles, clopidogrel has shown similar efficacy to ticagrelor and prasugrel [52].

Therefore, the investigators conducted the POPular Genetics trial [53], in which patients who required antiplatelet therapy were randomized to either a genotype-guided treatment or standard treatment, while the choice of antiplatelet drug was left to investigators discretion. However, patients carrying the CYP2C19\*2 or CYP2C19\*3 loss-of-function alleles in the genotype-guided group received ticagrelor or prasugrel, and noncarriers received clopidogrel. At 12 months, the primary outcome (death, MI, definite ST, stroke or major bleeding) occurred in 63 of the 1,242 patients (5.1%) in the genotype-guided group and 73 of the 1,246 patients (5.9%) in the standard treatment group ( $P_{\text{noninferiority}} < 0.001$ ). The bleeding outcome occurred in 122 patients (9.8%) in the genotype guided group and 156 patients (12.5%) in the standard treatment group ( $P_{\text{superiority}} = 0.04$ ). These data suggest that the CYP2C19 genetic testing to guide the selection of oral P2Y<sub>12</sub> inhibitor therapy in patients undergoing PCI was non-inferior to standard treatment with ticagrelor or prasugrel at 12 months in terms of thrombotic events

and resulted in a lower incidence of bleeding. A similar large scale RCT, the 5,300-patient TAILOR-PCI trial (NCT01742117) is awaited to add valuable information to this matter. The trial is in its final phase of recruitment, and if it will show the same results, current practice will be modified.

## **6. PCI for ACS and cardiogenic shock**

### **Microvascular obstruction**

Microvascular obstruction is common, affecting half of the patients with STEMI, associated with adverse outcomes, but there remains no therapy to prevent or treat this comorbidity. The T-TIME trial [54] aimed to determine whether a low-dose intracoronary fibrinolytic therapy with alteplase infused early after coronary reperfusion will reduce microvascular obstruction. A total of 440 patients presented with STEMI were randomized by 1:1:1 to either receive a placebo, alteplase 10 mg, or alteplase 20 mg. The primary outcome was the amount of microvascular obstruction (expressed as % left ventricular mass) demonstrated by contrast-enhanced cardiac magnetic resonance imaging (MRI) conducted from days 2 through 7 after enrollment. Results showed that the mean microvascular obstruction did not differ between the 20-mg alteplase and placebo groups (3.5% vs. 2.3%;  $P_{\text{superiority}}=0.32$ ) nor in the analysis of 10-mg alteplase versus placebo groups (2.6% vs. 2.3%;  $P_{\text{superiority}}=0.74$ ). The study findings disprove the treatment of low-dose intracoronary alteplase given during the primary PCI to reduce microvascular obstruction.

### **Timing of recanalization in patients with cardiac arrest**

Although clinically significant CAD is commonly observed in patients who have a cardiac arrest, the generally accepted consensus is that after resuscitation, the comatose patients who presented STEMI should undergo immediate CAG/PCI. Beside these patients, the role of immediate CAG/PCI after successful resuscitation is still uncertain [55], and the COACT trial [56] investigated this issue. A total of 552 patients who had cardiac arrest without signs of STEMI were randomly assigned to undergo immediate or delayed CAG/PCI until after neurologic recovery. At 90 days, 176 of 273 patients (64.5%) in the immediate angiography group and 178 of 265 patients (67.2%) in the delayed angiography group were alive ( $P_{\text{superiority}}=0.51$ ). These results suggested immediate angiography was not superior to a strategy of delayed angiography with respect to overall survival. One noteworthy limitation in the COACT trial is that after CAG, only less than 20% of overall participants were found to have presented ACS, and only 33% of the patients in the trial have undergone PCI. Thus, only a small fraction of participants in the trial would be affected by the timing of the PCI or the performance of the PCI. In the subgroup analyses, patients with age older than 70, or history of CAD appeared to benefit from immediate CAG/PCI ( $P_{\text{interaction}}<0.05$ , respectively). Therefore, the COACT trial should be interpreted cautiously, and further work is needed to guide the tailored treatment strategies for selected patients after cardiac arrest.

Patients with ACS who present initially with ST-elevation on the electrocardiogram but, subsequently, show complete normalization of the ST-segment and relief of symptoms before

reperfusion therapy are referred to as transient STEMI and pose a therapeutic challenge. It is unclear what the optimal timing of revascularization is for these patients and whether they should be treated with a STEMI-like or a NSTEMI-like invasive approach. The TRANSIENT trial [57] enrolled 142 patients to determine the effect of an immediate vs. a delayed invasive strategy. Overall, infarct size in transient STEMI is small and is not influenced by an immediate or delayed invasive strategy. Infarct size of the left ventricular myocardial mass measured by CMR at day 4 was 1.3% in the immediate group and 1.5% in the delayed invasive group ( $P_{\text{superiority}} = 0.48$ ). There was no difference in MACE, defined as death, reinfarction, or TVR at 30 days (2.9% vs. 2.8%,  $P_{\text{superiority}} = 1.00$ ). These results might indicate that among patients with transient STEMI, immediate invasive therapy does not have additional benefits in reducing infarct size over delayed invasive therapy. Although the trial was negative, these findings may help refining guidelines in this patient population.

### **Devices for cardiogenic shock and STEMI**

The role of intra-aortic balloon counterpulsation (IABP) in cardiogenic shock is still a subject of debate despite the neutral results of the 30 days results of the IABP-SHOCK II trial [58]. The 6-years result of the IABP SHOCK II trial [59] is now presented and exhibited that the mortality was not different between the IABP (197/297, 66.3%) and the control (197/294, 67.0%) group ( $P_{\text{superiority}} = 0.98$ ). Together with the negative result of the short-term, we can conclude that the use of IABP did not reduce early or late mortality, supporting current guideline recommendations of no routine use of IABP in cardiogenic shock.

The hemodynamic improvement from IABP may be too modest to affect mortality. It is unknown if a stronger mechanical support device such as Impella would have resulted in different outcomes. However, there are two retrospective analyses published this year investigating this question. One analysis showed that in patients with STEMI with cardiogenic shock, the use of an Impella was not associated with lower 30-day mortality compared with matched patients from the IABP-SHOCK II trial treated with an IABP or medical therapy [60], and the other analysis which included 48,306 patients, suggested that the use of Impella was associated with higher rates of adverse events and costs [61].

The cardioprotective remote ischemic conditioning stimulus can be applied using serial inflations and deflations of a pneumatic cuff placed on the upper arm or thigh to induce brief cycles of ischemia and reperfusion. Some clinical studies in patients with STEMI have showed that the remote ischemic conditioning increased myocardial salvage and reduced MI size by 20–30% when applied before or during reperfusion. The CONDI-2/ERIC-PPCI trial [62], with a RCT fashion, aimed to determine whether remote ischemic conditioning could reduce the incidence of cardiac death and hospitalization for heart failure at 12 months; however, the results are disappointing. At 12 months post-PCI, the primary endpoint (cardiac death or hospitalization for heart failure) occurred in 220 of 2569 (8.6%) patients in the control group and 239 of 2546 (9.4%) in the remote ischemic conditioning group ( $P_{\text{superiority}} = 0.32$ ), suggesting remote ischemic conditioning does not improve clinical outcomes.

### **7. Intracoronary imaging**

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## **Vulnerable atheromatous plaque detection**

So far, there are no prospective cohort data showing whether the cholesterol content within the coronary artery wall was predictive of future events. Lipid-rich plaque (LRP) is believed to be associated with ACS and can be detected by near-infrared spectroscopy (NIRS). In the LRP study [63], investigators aimed to establish the relationship between LRPs detected by combined NIRS-intravascular ultrasound imaging (IVUS) at unstented sites and subsequent coronary events from new culprit lesions. Patients with CAD who underwent cardiac catheterization were enrolled in the study, and their non-culprit segments were scanned by using NIRS-IVUS imaging. At the 2-year follow-up, the cumulative incidence of MACE (cardiac death or arrest, non-fatal MI, ACS, revascularization, and re-admission to hospital for angina) was 9% (n=103). On a patient level, the hazard ratio for MACE was 1.21 (95% CI 1.09-1.35;  $P_{\text{superiority}}=0.0004$ ) for each 100-unit increase in maxLCBI [Lipid Core Burden Index] 4mm. In patients with a maxLCBI 4mm more than 400, the HR for MACE was 2.18 (1.48-3.22;  $P_{\text{superiority}}<0.0001$ ). At the plaque level, the HR was 1.45 (1.30-1.60;  $P_{\text{superiority}}<0.0001$ ) for each 100-unit increase in maxLCBI 4mm. For segments with a maxLCBI 4mm more than 400, the HR for NC-MACE was 4.22 (2.39-7.45;  $P_{\text{superiority}}<0.0001$ ). The results might possibly suggest that combined NIRS-IVUS approach now adds an important tool to the diagnostic armamentarium of vulnerable plaques and vulnerable patients in clinical practice.

## **IVUS guidance of stent implantation**

The IVUS-XPL study was the first demonstration of the clinical benefit of IVUS guidance PCI in second-generation DES implantation. The 5-years result of the trial was recently presented [64], showing that when IVUS is used to guide PCI in long lesions, the clinical benefits over angiographic guidance extend up to 5 years. The primary endpoint (cardiac death, TLR-MI, ischemia-driven TLR) occurred in 36 patients (5.6%) receiving IVUS-guidance and in 70 patients (10.7%) receiving angiography-guidance ( $P=0.001$ ). The difference was mainly driven by a lower risk of TLR (31 [4.8%] vs. 55 [8.4%],  $P_{\text{superiority}}=0.007$ ). By landmark analysis, the primary endpoint between 1 and 5 years occurred in 17 patients (2.8%) receiving IVUS-guidance and in 31 patients (5.2%) receiving angiography-guidance ( $P_{\text{superiority}}=0.031$ ). These results reiterated beneficial effect of IVUS guidance and showed that the effect was not only sustained up to 5 years but also amplified between 1 and 5 years.

## **8. Technical approaches**

Some experienced femoral artery access interventionists still prefer this route for CAG or PCI. However, radial access has shown to reduce mortality and bleeding events, especially in patients with ACS [65]. The SURF trial [66] used a 2×2 factorial design to compare radial versus femoral and standard versus ultrasound guided puncture. A total of 1,388 patients were enrolled. The primary outcome was AQUIITY (Acute Catheterization and Urgent Intervention Triage strategy) major bleeding, MACE (death, stroke, MI or urgent TLR) and vascular complications at 30 days. Results showed that the transradial access reduced the primary outcome (RR 0.37, 95% CI: 0.17-0.81;  $P_{\text{superiority}}=0.013$ ),

mostly driven by AUCITY major bleeding (RR 0.34, 95% CI: 0.123-0.959;  $P_{\text{superiority}}=0.041$ ) when compared with the transfemoral approach. There was no difference in the primary outcome between the standard and ultrasound guidance for femoral artery access ( $P_{\text{superiority}}=0.76$ ). Ultrasound guidance, however, reduced mean access time (93 sec vs. 111 sec;  $p=0.009$ ), reduced the number of attempts (1.47 vs. 1.9;  $P_{\text{superiority}}<0.0001$ ), vene-puncture occurrence (4.1% vs. 9.2%;  $P_{\text{superiority}}<0.0001$ ) and improved the success rate of difficult access (4.5% vs. 9.2%;  $p=0.0007$ ) and the first-pass success (73% vs. 59.7%;  $p<0.0001$ ). The take-home message of the SURF trial is clear -with or without the ultrasound guidance, transradial access shall still be the preferred vascular access route.

Intravascular lithotripsy (IVL) is a novel technology, based on an established treatment strategy for renal calculi, in which multiple lithotripsy emitters mounted on a traditional catheter platform deliver localized pulsatile sonic pressure waves to modify vascular calcium circumferentially. The recently published DISRUPT CAD II study [67] proved the safety and effectiveness of IVL for vessel preparation of severe CAC in stenotic de novo coronary lesions. One hundred and twenty patients with severe CAC with a clinical indication for revascularization were enrolled in the trial. The post-IVL angiographic acute luminal gain was  $0.83\pm0.47$  mm, and residual stenosis was  $32.7\pm10.4\%$ , which further decreased to  $7.8\pm7.1\%$  after stent implantation. The primary endpoint (cardiac death, target MI and revascularization) occurred in 5.8% of patients, consisting of 7 non-Q-wave myocardial infarctions. There was no procedural abrupt closure, slow or no-reflow, or perforations. The ongoing DISRUPT CAD III study is expected to provide further evidence about the safety and efficacy of IVL in the treatment of calcified lesions (NCT03595176).

## Conclusion and Perspectives

In 2019, robust evidence highlights the short- and long-term efficacy of the second-generation DES. The evidence that reinforces the concept of “short DAPT” has grown. The long-awaited ISCHEMIA trial confirmed invasive strategy cannot reduce hard endpoints but has durable improvements in angina control and quality of life. Astonishing advances have taken place, reshaped our daily practice, and is expected to improve the quality of life and the long-term survival of patients with CAD.



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## Figure Legends:

Figure 1: A few of the important trials reported in 2019

Figure 2: Primary endpoint of EXCEL, NOBLE and SYNTAXES trials

A: the SYNTAXES study; B: the FREEDOM Follow-On study; C: the EXCEL study; D: the NOBLE study;

Figure 3: The duration of DAPT and the outcomes

Table 1 Competition between stents

## Reference

1. Kandzari DE, Mauri L, Koolen JJ, Massaro JM, Doros G, Garcia-Garcia HM, Bennett J, Roguin A, Gharib EG, Cutlip DE, Waksman R. Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a randomised trial. *The Lancet*.2017;390:1843-1852.
2. Iglesias JF, Muller O, Heg D, Roffi M, Kurz DJ, Moarof I, Weilenmann D, Kaiser C, Tapponnier M, Stortecky S, Losdat S, Eeckhout E, Valgimigli M, Odutayo A, Zwahlen M, Jüni P, Windecker S, Pilgrim T. Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in patients with ST-segment elevation myocardial infarction (BIOSTEMI): a single-blind, prospective, randomised superiority trial. *The Lancet*.2019;394:1243-1253.
3. Zaman A, De Winter RJ, Kogame N, Chang CC, Modolo R, Spitzer E, Tonino P, Hofma S, Zurakowski A, Smits PC, Prokopcuk J, Moreno R, Choudhury A, Petrov I, Cequier A, Kukreja N, Hoyer A, Iniguez A, Ungi I, Serra A, Gil RJ, Walsh S, Tonev G, Mathur A, Merkely B, Colombo A, Ijsselmuiden S, Soliman O, Kaul U, Onuma Y, Serruys PW. Safety and efficacy of a sirolimus-eluting coronary stent with ultra-thin strut for treatment of atherosclerotic lesions (TALENT): a prospective multicentre randomised controlled trial. *The Lancet*.2019;393:987-997.
4. Rozemeijer R, Stein M, Voskuil M, Van Den Bor R, Frambach P, Pereira B, Koudstaal S, Leenders GE, Timmers L, Rittersma SZ, Kraaijeveld AO, Agostoni P, Roes KC, Doevendans PA, Stella PR, Recre8 Study I. Randomized All-Comers Evaluation of a Permanent Polymer Zotarolimus-Eluting Stent Versus a Polymer-Free Amphilimus-Eluting Stent. *Circulation*.2019;139:67-77.
5. Maeng M, Christiansen EH, Raungaard B, Kahlert J, Terkelsen CJ, Kristensen SD, Carstensen S, Aaroe J, Jensen SE, Villadsen AB, Lassen JF, Thim T, Eftekhari A, Veien KT, Hansen KN, Junker A, Botker HE, Jensen LO, Investigators SOV. Everolimus-Eluting Versus Biolimus-Eluting Stents With Biodegradable Polymers in Unselected Patients Undergoing Percutaneous Coronary Intervention: A Randomized Noninferiority Trial With 1-Year Follow-Up (SORT OUT VIII Trial). *JACC Cardiovasc Interv*.2019;12:624-633.
6. Valdes-Chavarri M, Kedev S, Neskovic AN, Moris De La Tassa C, Zivkovic M, Trillo Nouche R, Vazquez Gonzalez N, Bartorelli AL, Antonucci D, Tamburino C, Colombo A, Abizaid AA, Mcfadden E, Garcia-Garcia HM, Milasinovic D, Stankovic G. Randomised evaluation of a novel biodegradable polymer-based sirolimus-eluting stent in ST-segment elevation myocardial infarction: the MASTER study. *EuroIntervention*.2019;14:e1836-e1842.
7. Saito S, Toelg R, Witzembichler B, Haude M, Masotti M, Salmeron R, Witkowski A, Uematsu M, Takahashi A, Waksman R, Slagboom T. BIOFLOW-IV, a randomised, intercontinental, multicentre study to assess the safety and effectiveness of the Orsiro sirolimus-eluting stent in the treatment of subjects with de novo coronary artery lesions: primary outcome target vessel failure at 12 months. *EuroIntervention*.2019;15:e1006-e1013.
8. Kufner S, Joner M, Thannheimer A, Hoppmann P, Ibrahim T, Mayer K, Cassese S, Laugwitz KL, Schunkert H, Kastrati A, Byrne RA, Investigators I-T. Ten-Year Clinical Outcomes From a Trial of Three Limus-Eluting Stents With Different Polymer Coatings in Patients With Coronary Artery Disease. *Circulation*.2019;139:325-333.
9. Raber L, Yamaji K, Kelbaek H, Engstrom T, Baumbach A, Roffi M, Von Birgelen C, Taniwaki M, Moschovitis A, Zaugg S, Ostojic M, Pedrazzini G, Karagiannis-Voules DA, Luscher TF, Kornowski R, Tuller D, Vukcevic V, Heg D, Windecker S. Five-year clinical outcomes and intracoronary imaging findings of the COMFORTABLE AMI trial: randomized comparison of biodegradable polymer-based biolimus-eluting stents with bare-metal stents in patients with acute ST-segment elevation myocardial infarction. *Eur Heart J*.2019;40:1909-1919.
10. Chichareon P, Modolo R, Collet C, Tenekecioglu E, Vink MA, Oh PC, Ahn JM, Musto C, Diaz De La Llera LS, Cho YS, Violini R, Park SJ, Suryapranata H, Piek JJ, De Winter RJ, Wykrzykowska JJ, Spaulding C, Kang WC, Slagboom T, Hofma SH, Wijnbergen IF, Di Lorenzo E, Pijls NH, Raber L, Brugaletta S, Sabate M, Stoll HP, Stone GW, Windecker S, Onuma Y, Serruys PW. Efficacy and Safety of Stents in ST-Segment Elevation Myocardial Infarction. *J Am Coll Cardiol*.2019;74:2572-2584.
11. Piccolo R, Bonaa KH, Efthimiou O, Varenne O, Baldo A, Urban P, Kaiser C, Remkes W, Raber L, De Belder A, Van 'T Hof AWJ, Stankovic G, Lemos PA, Wilsaard T, Reifart J, Rodriguez AE, Ribeiro EE, Serruys P, Abizaid A, Sabate M, Byrne RA, De La Torre Hernandez JM, Wijns W, Juni P, Windecker S, Valgimigli M, Coronary Stent Trialists C. Drug-eluting or bare-metal stents for percutaneous coronary

- intervention: a systematic review and individual patient data meta-analysis of randomised clinical trials. *Lancet*.2019;393:2503-2510.
12. Jeger RV, Farah A, Ohlow M-A, Mangner N, Möbius-Winkler S, Leibundgut G, Weilenmann D, Wöhrle J, Richter S, Schreiber M, Mahfoud F, Linke A, Stephan F-P, Mueller C, Rickenbacher P, Coslovsky M, Gilgen N, Osswald S, Kaiser C, Scheller B, Buser P, Kühne M, Zellweger M, Sticherling C, Wein B, Twerenbold R, Fahrni G, Plicht B, Struck B, Önal I, Cremers B, Clever Y, Ewen S, Schirmer S, Böhm M, Wagner A, Lauer B, Stachel G, Höllriegel R, Winzer E, Rickli H, Ammann P, Haager P, Trachsel L, Joerg L, Nüssli D, Roelli H, Maeder M, Rohner F, Markovic S, Paliskyte R, Buckert D, Awad B, Erne P, Jamshidi P, Cuculi F, Kapos I, Toggweiler S, Riede F, Pörner T, Lenk K, Noutsias M, Surber R, Dannberg G, Franz M, Otto S, Zweiker R, Niederl E, Perl S, Pieske B, Schmidt A, Luha O, Von Lewinski D, Krackhardt F, Kherad B, Jerichow T, Butter C, Neuss M, Tambor G, Hölschermann F, Bruch L, Winkler S, Lenz C, Seidel M, Keweloh B, Röttgen A, Bohl S, Wolf A, Hoffmann A. Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial. *The Lancet*.2018;392:849-856.
  13. Rissanen TT, Uskela S, Eranen J, Mantyla P, Olli A, Romppanen H, Siljander A, Pietila M, Minkkinen MJ, Tervo J, Karkkainen JM, Investigators DT. Drug-coated balloon for treatment of de-novo coronary artery lesions in patients with high bleeding risk (DEBUT): a single-blind, randomised, non-inferiority trial. *Lancet*.2019;394:230-239.
  14. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO, Group ESCSD. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*.2019;40:87-165.
  15. Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrie D, Naber C, Lipiecki J, Richardt G, Iniguez A, Brunel P, Valdes-Chavarri M, Garot P, Talwar S, Berland J, Abdellaoui M, Eberli F, Oldroyd K, Zambahari R, Gregson J, Greene S, Stoll HP, Morice MC, Investigators LF. Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk. *N Engl J Med*.2015;373:2038-2047.
  16. Vos NS, Fagel ND, Amoroso G, Herrman J-PR, Patterson MS, Piers LH, Van Der Schaaf RJ, Slagboom T, Vink MA. Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stent in Acute Myocardial Infarction. *JACC: Cardiovascular Interventions*.2019;12:1691-1699.
  17. Giaccopo D, Alfonso F, Xu B, Claessen B, Adriaenssens T, Jensen C, Perez-Vizcayno MJ, Kang DY, Degenhardt R, Pleva L, Baan J, Cuesta J, Park DW, Schunkert H, Collieran R, Kukla P, Jimenez-Quevedo P, Unverdorben M, Gao R, Naber CK, Park SJ, Henriques JPS, Kastrati A, Byrne RA. Paclitaxel-coated balloon angioplasty vs. drug-eluting stenting for the treatment of coronary in-stent restenosis: a comprehensive, collaborative, individual patient data meta-analysis of 10 randomized clinical trials (DAEDALUS study). *Eur Heart J*.2019;doi:10.1093/eurheartj/ehz594
  18. Thuijs DJFM, Kappetein AP, Serruys PW, Mohr F-W, Morice M-C, Mack MJ, Holmes DR, Curzen N, Davierwala P, Noack T, Milojevic M, Dawkins KD, Da Costa BR, Jüni P, Head SJ, Casselman F, De Bruyne B, Høj Christiansen E, Ruiz-Nodar JM, Vermeersch P, Schultz W, Sabaté M, Guagliumi G, Grubitzsch H, Stangl K, Darremont O, Bentala M, Den Heijer P, Preda I, Stoler R, Mack MJ, Szerafin T, Buckner JK, Guber MS, Verberkmoes N, Akca F, Feldman T, Beyersdorf F, Drieghe B, Oldroyd K, Berg G, Jeppsson A, Barber K, Wolschleger K, Heiser J, Van Der Harst P, Mariani MA, Reichenspurner H, Stark C, Laine M, Ho PC, Chen JC, Zelman R, Horwitz PA, Bochenek A, Krauze A, Grothusen C, Dudek D, Heyrich G, Davierwala P, Noack T, Kolh P, Legrand V, Coelho P, Ensminger S, Nasser B, Ingemansson R, Olivecrona G, Escaned J, Guera R, Berti S, Morice M-C, Chieffo A, Burke N, Mooney M, Spolaor A, Hagl C, Nábauer M, Suttorp MJ, Stine RA, McGarry T, Lucas S, Endresen K, Taussig A, Accola K, Canosi U, Horvath I, Cannon L, Talbott JD, Akins CW, Kramer R, Aschermann M, Killinger W, Narbutė I, Holmes DR, Burzotta F, Bogers A, Zijlstra F, Eltchaninoff H, Berland J, Stefanini G, Cruz Gonzalez I, Hoppe U, Kiesz S, Gora B, Ahlsson A, Corbascio M, Bilfinger T, Carrie D, Tchétché D, Hauptman K-E, Stahle E, James S, Sandner S, Laufer G, Lang I, Witkowski A, Thourani V, Suryapranata H, Redwood S, Knight C, Mccarthy P, Curzen N, De Belder A, Banning A, Gershlick A. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *The Lancet*.2019;394:1325-1334.
  19. Farkouh ME, Domanski M, Dangas GD, Godoy LC, Mack MJ, Siami FS, Hamza TH, Shah B, Stefanini GG, Sidhu MS, Tanguay JF, Ramanathan K, Sharma SK, French J, Hueb W, Cohen DJ, Fuster V, Investigators FF-OS. Long-Term Survival Following Multivessel Revascularization in Patients With Diabetes: The FREEDOM Follow-On Study. *J Am Coll Cardiol*.2019;73:629-638.

20. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, Yang M, Cohen DJ, Rosenberg Y, Solomon SD, Desai AS, Gersh BJ, Magnuson EA, Lansky A, Boineau R, Weinberger J, Ramanathan K, Sousa JE, Rankin J, Bhargava B, Buse J, Hueb W, Smith CR, Muratov V, Bansilal S, King S, 3rd, Bertrand M, Fuster V, Investigators FT. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med.*2012;367:2375-2384.
21. Makikallio T, Holm NR, Lindsay M, Spence MS, Erglis A, Menown IB, Trovik T, Eskola M, Romppanen H, Kellerth T, Ravkilde J, Jensen LO, Kalinauskas G, Linder RB, Pentikainen M, Hervold A, Banning A, Zaman A, Cotton J, Eriksen E, Margus S, Sorensen HT, Nielsen PH, Niemela M, Kervinen K, Lassen JF, Maeng M, Oldroyd K, Berg G, Walsh SJ, Hanratty CG, Kumsars I, Stradins P, Steigen TK, Frobert O, Graham AN, Endresen PC, Corbascio M, Kajander O, Trivedi U, Hartikainen J, Anttila V, Hildick-Smith D, Thuesen L, Christiansen EH, Investigators NS. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. *Lancet.*2016;388:2743-2752.
22. Boden WE, O'rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, Chaitman BR, Shaw L, Gosselin G, Nawaz S, Title LM, Gau G, Blaustein AS, Booth DC, Bates ER, Spertus JA, Berman DS, Mancini GB, Weintraub WS, Group CTR. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med.*2007;356:1503-1516.
23. Al-Lamee R, Thompson D, Dehbi H-M, Sen S, Tang K, Davies J, Keeble T, Mielewicz M, Kaprielian R, Malik IS, Nijjer SS, Petraco R, Cook C, Ahmad Y, Howard J, Baker C, Sharp A, Gerber R, Talwar S, Assomull R, Mayet J, Wensel R, Collier D, Shun-Shin M, Thom SA, Davies JE, Francis DP, Al-Lamee R, Thompson D, Sen S, Tang K, Davies J, Keeble T, Kaprielian R, Malik IS, Nijjer SS, Petraco R, Cook C, Ahmad Y, Howard J, Shun-Shin M, Sethi A, Baker C, Sharp A, Ramrakha P, Gerber R, Talwar S, Assomull R, Foale R, Mayet J, Wensel R, Thom SA, Davies JE, Francis DP, Khamis R, Hadjiloizou N, Khan M, Kooner J, Bellamy M, Mikhail G, Clifford P, O'kane P, Levy T, Swallow R. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. *The Lancet.*2018;391:31-40.
24. The homesite of the ISCHEMIA trial <https://www.ischemiatrial.org>
25. President's Message to Members on the ISCHEMIA Trial.
26. Greenwood JP, Maredia N, Younger JF, Brown JM, Nixon J, Everett CC, Bijsterveld P, Ridgway JP, Radjenovic A, Dickinson CJ, Ball SG, Plein S. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. *Lancet.*2012;379:453-460.
27. Nagel E, Greenwood JP, Mccann GP, Bettencourt N, Shah AM, Hussain ST, Perera D, Plein S, Bucciarelli-Ducci C, Paul M, Westwood MA, Marber M, Richter WS, Puntmann VO, Schwenke C, Schulz-Menger J, Das R, Wong J, Hausenloy DJ, Steen H, Berry C, Investigators M-I. Magnetic Resonance Perfusion or Fractional Flow Reserve in Coronary Disease. *N Engl J Med.*2019;380:2418-2428.
28. Mehta SR, Wood DA, Storey RF, Mehran R, Baine KR, Nguyen H, Meeks B, Di Pasquale G, Lopez-Sendon J, Faxon DP, Mauri L, Rao SV, Feldman L, Steg PG, Avezum A, Sheth T, Pinilla-Echeverri N, Moreno R, Campo G, Wrigley B, Kedev S, Sutton A, Oliver R, Rodes-Cabau J, Stankovic G, Welsh R, Lavi S, Cantor WJ, Wang J, Nakamya J, Bangdiwala SI, Cairns JA, Committee CTS, Investigators. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N Engl J Med.*2019;381:1411-1421.
29. Burzotta F, Lassen JF, Banning AP, Lefevre T, Hildick-Smith D, Chieffo A, Darremont O, Pan M, Chatzizisis YS, Albiero R, Louvard Y, Stankovic G. Percutaneous coronary intervention in left main coronary artery disease: the 13th consensus document from the European Bifurcation Club. *EuroIntervention.*2018;14:112-120.
30. Chen SL, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, Jiang T, Tao L, Zeng H, Li L, Xia Y, Gao C, Santoso T, Paiboon C, Wang Y, Kwan TW, Ye F, Tian N, Liu Z, Lin S, Lu C, Wen S, Hong L, Zhang Q, Sheiban I, Xu Y, Wang L, Rab TS, Li Z, Cheng G, Cui L, Leon MB, Stone GW. Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions: DKCRUSH-V Randomized Trial. *J Am Coll Cardiol.*2017;70:2605-2617.
31. Chen X, Li X, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, Santoso T, Paiboon C, Kwan TW, Sheiban I, Leon MB, Stone GW, Chen SL, Investigators D-V. 3-Year Outcomes of the DKCRUSH-V Trial Comparing DK Crush With Provisional Stenting for Left Main Bifurcation Lesions. *JACC Cardiovasc Interv.*2019;12:1927-1937.
32. Lee SW, Lee PH, Ahn JM, Park DW, Yun SC, Han S, Kang H, Kang SJ, Kim YH, Lee CW, Park SW, Hur SH, Rha SW, Her SH, Choi SW, Lee BK, Lee NH, Lee JY, Cheong SS, Kim MH, Ahn YK, Lim SW, Lee SG,

- Hiremath S, Santoso T, Udayachalerm W, Cheng JJ, Cohen DJ, Muramatsu T, Tsuchikane E, Asakura Y, Park SJ. Randomized Trial Evaluating Percutaneous Coronary Intervention for the Treatment of Chronic Total Occlusion. *Circulation*.2019;139:1674-1683.
33. Capodanno D, Mehran R, Valgimigli M, Baber U, Windecker S, Vranckx P, Dangas G, Rollini F, Kimura T, Collet JP, Gibson CM, Steg PG, Lopes RD, Gwon HC, Storey RF, Franchi F, Bhatt DL, Serruys PW, Angiolillo DJ. Aspirin-free strategies in cardiovascular disease and cardioembolic stroke prevention. *Nat Rev Cardiol*.2018;15:480-496.
  34. Vranckx P, Valgimigli M, Jüni P, Hamm C, Steg PG, Heg D, Van Es GA, Mcfadden EP, Onuma Y, Van Meijeren C, Chichareon P, Benit E, Möllmann H, Janssens L, Ferrario M, Moschovitis A, Zurakowski A, Dominici M, Van Geuns RJ, Huber K, Slagboom T, Serruys PW, Windecker S, Abdellaoui M, Adlam D, Akin I, Albarran Gonzalez-Trevilla A, Almeida M, Alves Lemos Neto P, Aminian A, Anderson R, Andreae R, Angioi M, Asano T, Barbato E, Barlis P, Barraud P, Benit E, Bertrand O, Beygui F, Bolognese L, Botelho R, Bouwman C, Bressers M, Brunel P, Buszman P, Buysschaert I, Canas Da Silva P, Carrie D, Cequier A, Chichareon P, Chin Chang C, Chowdhary S, Collet C, Colombo A, Cotton J, Cruz Ferreira R, Curello S, Curzen N, De Bot J, De Vreede T, Delle Karth G, Dijkstra L, Dominici M, Édes I, Eeckhout E, Eitel I, Faluközy J, Fath-Ordoubadi F, Ferrario M, Fontos G, Francisco Diaz J, Freitas Quintella E, Frey B, Friedrich G, Galasko G, Galuszka G, Gama Ribeiro V, Garg S, Gargiulo G, Geisler T, Gelev V, Ghandilyan A, Goicolea J, Gori T, Gragnano F, Guimarães A, Hamm C, Haude M, Heg D, Heijke P, Hernández Antolin RA, Hildick-Smith D, Hillen D, Hoekman I, Hofma S, Holmvang L, Hoole S, Horváth I, Huber K, Hugense A, Ibrahim K, Iñiguez A, Isaaz K, Jambrik Z, Janssens L, Jasionowicz P, Jonk J, Jung W, Jüni P, Katagiri Y, Kogame N, Koh TH, Koning R, Konteva M, Kőszegi Z, Krackhardt F, Kreuger Y, Kukreja N, Ladan B, Lantelme P, Leandro S, Leibundgut G, Liebetrau C, Lindeboom W, Macaya Miguel C, Mach F, Magro M, Maillard L, Manavifar N, Mauri L, Mcfadden E, Merkely B, Miyazaki Y, Młodziankowski A, Moccetti T, Modolo R, Möllman H, Morelle J-F, Moschovitis A, Munnndt Ottesen M, Muurling M, Naber CK, Neumann F-J, Oldroyd K, Ong P, Onuma Y, Palsrok S, Petrov I, Plante S, Prokopcuk J, Rademaker-Havinga T, Raffel C, Rensing B, Roffi M, Royaards K-J, Sabate M, Schächinger V, Seidler T, Serra Peñaranda A, Serruys P, Sikarulidze L, Slagboom T, Soliman OI, Sousa A, Spitzer E, Stables R, Steg G, Steinwender C, Subkovas E, Suryapranata H, Takahashi K, Talwar S, Teiger E, Ter Weele A, Teurlings E, Thury A, Tijssen J, Tonev G, Trendafilova-Lazarova D, Tumscitz C, Umans V, Ungi I, Valkov V, Van Der Harst P, Van Geuns RJ, Van Meijeren C, Vassilev D, Velchev V, Velthuisen E, Verheugt F, Vlack N, Vom Dahl J, Vrolix M, Walsh S, Werner N, Windecker S, Witsenburg M, Zaman A, Žmudka K, Zrenner B, Zurakowski A, Zweiker R. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomised superiority trial. *The Lancet*.2018;392:940-949.
  35. Vranckx P, Valgimigli M, Windecker S, Steg PG, Hamm C, Juni P, Garcia-Garcia HM, Van Es GA, Serruys PW. Long-term ticagrelor monotherapy versus standard dual antiplatelet therapy followed by aspirin monotherapy in patients undergoing biolimus-eluting stent implantation: rationale and design of the GLOBAL LEADERS trial. *EuroIntervention*.2016;12:1239-1245.
  36. Watanabe H, Domei T, Morimoto T, Natsuaki M, Shiomi H, Toyota T, Ohya M, Suwa S, Takagi K, Nanasato M, Hata Y, Yagi M, Suematsu N, Yokomatsu T, Takamisawa I, Doi M, Noda T, Okayama H, Seino Y, Tada T, Sakamoto H, Hibi K, Abe M, Kawai K, Nakao K, Ando K, Tanabe K, Ikari Y, Hanaoka KI, Morino Y, Kozuma K, Kadota K, Furukawa Y, Nakagawa Y, Kimura T, Investigators S-. Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI: The STOPDAPT-2 Randomized Clinical Trial. *JAMA*.2019;321:2414-2427.
  37. Takahashi K, Serruys PW, Chichareon P, Chang CC, Tomaniak M, Modolo R, Kogame N, Magro M, Chowdhary S, Eitel I, Zweiker R, Ong P, Ottesen MM, Tijssen JGP, Wykrzykowska JJ, De Winter RJ, Garg S, Stoll HP, Hamm C, Steg PG, Onuma Y, Valgimigli M, Vranckx P, Carrie D, Windecker S. Efficacy and Safety of Ticagrelor Monotherapy in Patients Undergoing Multivessel PCI. *J Am Coll Cardiol*.2019;74:2015-2027.
  38. Serruys PW, Takahashi K, Chichareon P, Kogame N, Tomaniak M, Modolo R, Chang CC, Komiyama H, Soliman O, Wykrzykowska JJ, De Winter RJ, Ferrario M, Dominici M, Buszman P, Bolognese L, Tumscitz C, Benit E, Stoll HP, Hamm C, Steg PG, Onuma Y, Juni P, Windecker S, Vranckx P, Colombo A, Valgimigli M. Impact of long-term ticagrelor monotherapy following 1-month dual antiplatelet therapy in patients who underwent complex percutaneous coronary intervention: insights from the Global Leaders trial. *Eur Heart J*.2019;40:2595-2604.

39. Takahashi K, Chichareon P, Modolo R, Kogame N, Chang CC, Tomaniak M, Moschovitis A, Curzen N, Haude M, Jung W, Holmvang L, Garg S, Tijssen JGP, Wykrzykowska JJ, De Winter RJ, Hamm C, Steg PG, Stoll HP, Onuma Y, Valgimigli M, Vranckx P, Windecker S, Serruys PW. Impact of Ticagrelor Monotherapy on Two-Year Clinical Outcomes in Patients with Long Stenting: A Post Hoc Analysis of the Global Leaders Trial. *EuroIntervention*.2019;doi:10.4244/EIJ-D-19-00498
40. Kogame N, Chichareon P, De Wilder K, Takahashi K, Modolo R, Chang CC, Tomaniak M, Komiyama H, Chieffo A, Colombo A, Garg S, Louvard Y, Juni P, P GS, Hamm C, Vranckx P, Valgimigli M, Windecker S, Stoll HP, Onuma Y, Janssens L, Serruys PW. Clinical relevance of ticagrelor monotherapy following 1-month dual antiplatelet therapy after bifurcation percutaneous coronary intervention: Insight from GLOBAL LEADERS trial. *Catheter Cardiovasc Interv*.2019;doi:10.1002/ccd.28428
41. Tomaniak M, Chichareon P, Modolo R, Takahashi K, Chang CC, Kogame N, Spitzer E, Buszman PE, Van Geuns RM, Valkov V, Steinwender C, Geisler T, Prokopczuk J, Sabate M, Zmudka K, Rademaker-Havinga T, Tijssen JGP, Juni P, Hamm C, Steg PG, Onuma Y, Vranckx P, Valgimigli M, Windecker S, Baber U, Anderson R, Dominici M, Serruys PW. Ticagrelor Monotherapy Beyond One Month after PCI in ACS or Stable CAD in Elderly Patients Aged Above 75 Years: a Prespecified Analysis of the Randomized GLOBAL LEADERS Trial. *EuroIntervention*.2019;doi:10.4244/EIJ-D-19-00699
42. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P, Birmingham M, Janus J, Burton P, Van Eickels M, Korjian S, Daaboul Y, Lip GY, Cohen M, Husted S, Peterson ED, Fox KA. Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI. *N Engl J Med*.2016;375:2423-2434.
43. Cannon CP, Bhatt DL, Oldgren J, Lip GYH, Ellis SG, Kimura T, Maeng M, Merkely B, Zeymer U, Gropper S, Nordaby M, Kleine E, Harper R, Manassie J, Januzzi JL, Ten Berg JM, Steg PG, Hohnloser SH, Committee R-DPS, Investigators. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. *N Engl J Med*.2017;377:1513-1524.
44. Angiolillo DJ, Goodman SG, Bhatt DL, Eikelboom JW, Price MJ, Moliterno DJ, Cannon CP, Tanguay JF, Granger CB, Mauri L, Holmes DR, Gibson CM, Faxon DP. Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention. *Circulation*.2018;138:527-536.
45. Lip GYH, Collet JP, Haude M, Huber K. Management of antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI: A Summary of the Joint Consensus Document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). *Eur Heart J*.2018;39:2847-2850.
46. Vranckx P, Valgimigli M, Eckardt L, Tijssen J, Lewalter T, Gargiulo G, Batushkin V, Campo G, Lysak Z, Vakaliuk I, Milewski K, Laeis P, Reimitz PE, Smolnik R, Zierhut W, Goette A. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. *Lancet*.2019;394:1335-1343.
47. Lopes RD, Heizer G, Aronson R, Vora AN, Massaro T, Mehran R, Goodman SG, Windecker S, Darius H, Li J, Averkov O, Bahit MC, Berwanger O, Budaj A, Hijazi Z, Parkhomenko A, Sinnaeve P, Storey RF, Thiele H, Vinereanu D, Granger CB, Alexander JH, Investigators A. Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation. *N Engl J Med*.2019;380:1509-1524.
48. Mehta SR. Refining Antithrombotic Therapy for Atrial Fibrillation and Acute Coronary Syndromes or PCI. *N Engl J Med*.2019;380:1580-1581.
49. Yasuda S, Kaikita K, Akao M, Ako J, Matoba T, Nakamura M, Miyauchi K, Hagiwara N, Kimura K, Hirayama A, Matsui K, Ogawa H, Investigators A. Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease. *N Engl J Med*.2019;381:1103-1113.
50. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, Juni P, Kastrati A, Kolh P, Mauri L, Montalescot G, Neumann FJ, Petricevic M, Roffi M, Steg PG, Windecker S, Zamorano JL, Levine GN, Group ESCSD, Guidelines ESCCFP, Societies ESCNC. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*.2018;39:213-260.
51. Schupke S, Neumann FJ, Menichelli M, Mayer K, Bernlochner I, Wohrle J, Richardt G, Liebetrau C, Witzensbichler B, Antoniucci D, Akin I, Bott-Flugel L, Fischer M, Landmesser U, Katus HA, Sibbing D, Seyfarth M, Janisch M, Boncompagni D, Hilz R, Rottbauer W, Okrojek R, Mollmann H, Hochholzer W,

- Migliorini A, Cassese S, Mollo P, Xhepa E, Kufner S, Strehle A, Leggewie S, Allali A, Ndrepepa G, Schuhlen H, Angiolillo DJ, Hamm CW, Hapfelmeier A, Tolg R, Trenk D, Schunkert H, Laugwitz KL, Kastrati A, Investigators I-RT. Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes. *N Engl J Med*.2019;381:1524-1534.
52. Mega JL, Close SL, Wiviott SD, Shen L, Walker JR, Simon T, Antman EM, Braunwald E, Sabatine MS. Genetic variants in ABCB1 and CYP2C19 and cardiovascular outcomes after treatment with clopidogrel and prasugrel in the TRITON-TIMI 38 trial: a pharmacogenetic analysis. *Lancet*.2010;376:1312-1319.
  53. Claassens DMF, Vos GJA, Bergmeijer TO, Hermanides RS, Van 't Hof AWJ, Van Der Harst P, Barbato E, Morisco C, Tjon Joe Gin RM, Asselbergs FW, Mosterd A, Herrman JR, Dewilde WJM, Janssen PWA, Kelder JC, Postma MJ, De Boer A, Boersma C, Deneer VHM, Ten Berg JM. A Genotype-Guided Strategy for Oral P2Y12 Inhibitors in Primary PCI. *N Engl J Med*.2019;381:1621-1631.
  54. Mccartney PJ, Eteiba H, Maznyczka AM, Mcentegart M, Greenwood JP, Muir DF, Chowdhary S, Gershlick AH, Appleby C, Cotton JM, Wragg A, Curzen N, Oldroyd KG, Lindsay M, Rocchiccioli JP, Shaukat A, Good R, Watkins S, Robertson K, Malkin C, Martin L, Gillespie L, Ford TJ, Petrie MC, Macfarlane PW, Tait RC, Welsh P, Sattar N, Weir RA, Fox KA, Ford I, Mcconnachie A, Berry C, Group TT. Effect of Low-Dose Intracoronary Alteplase During Primary Percutaneous Coronary Intervention on Microvascular Obstruction in Patients With Acute Myocardial Infarction: A Randomized Clinical Trial. *JAMA*.2019;321:56-68.
  55. Abella BS, Gaieski DF. Coronary Angiography after Cardiac Arrest - The Right Timing or the Right Patients? *N Engl J Med*.2019;380:1474-1475.
  56. Lemkes JS, Janssens GN, Van Der Hoeven NW, Jewbali LSD, Dubois EA, Meuwissen M, Rijpsma TA, Bosker HA, Blans MJ, Bleeker GB, Baak R, Vlachoianis GJ, Eikemans BJW, Van Der Harst P, Van Der Horst ICC, Voskuil M, Van Der Heijden JJ, Beishuizen A, Stoel M, Camaro C, Van Der Hoeven H, Henriques JP, Vlaar APJ, Vink MA, Van Den Bogaard B, Heestermaans T, De Ruijter W, Delnoij TSR, Crijns H, Jessurun GAJ, Oemrawsingh PV, Gosselink MTM, Plomp K, Magro M, Elbers PWG, Van De Ven PM, Oudemans-Van Straaten HM, Van Royen N. Coronary Angiography after Cardiac Arrest without ST-Segment Elevation. *N Engl J Med*.2019;380:1397-1407.
  57. Lemkes JS, Janssens GN, Van Der Hoeven NW, Van De Ven PM, Marques KMJ, Nap A, Van Leeuwen MaH, Appelman YEA, Knaapen P, Verouden NJW, Allaart CP, Brinckman SL, Saraber CE, Plomp KJ, Timmer JR, Kedhi E, Hermanides RS, Meuwissen M, Schaap J, Van Der Weerd AP, Van Rossum AC, Nijveldt R, Van Royen N. Timing of revascularization in patients with transient ST-segment elevation myocardial infarction: a randomized clinical trial. *Eur Heart J*.2019;40:283-291.
  58. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennerdsdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Bohm M, Ebel H, Schneider S, Schuler G, Werdan K, Investigators I-SIT. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*.2012;367:1287-1296.
  59. Thiele H, Zeymer U, Thelemann N, Neumann FJ, Hausleiter J, Abdel-Wahab M, Meyer-Saraei R, Fuernau G, Eitel I, Hambrecht R, Bohm M, Werdan K, Felix SB, Hennerdsdorf M, Schneider S, Ouarrak T, Desch S, De Waha-Thiele S, Investigators IIT. Intraaortic Balloon Pump in Cardiogenic Shock Complicating Acute Myocardial Infarction: Long-Term 6-Year Outcome of the Randomized IABP-SHOCK II Trial. *Circulation*.2018;doi:10.1161/CIRCULATIONAHA.118.038201
  60. Schrage B, Ibrahim K, Loehn T, Werner N, Sinning JM, Pappalardo F, Pieri M, Skurk C, Lauten A, Landmesser U, Westenfeld R, Horn P, Pauschinger M, Eckner D, Twerenbold R, Nordbeck P, Salinger T, Abel P, Empen K, Busch MC, Felix SB, Sieweke JT, Moller JE, Pareek N, Hill J, Maccarthy P, Bergmann MW, Henriques JPS, Mobius-Winkler S, Schulze PC, Ouarrak T, Zeymer U, Schneider S, Blankenberg S, Thiele H, Schafer A, Westermann D. Impella Support for Acute Myocardial Infarction Complicated by Cardiogenic Shock. *Circulation*.2019;139:1249-1258.
  61. Amin AP, Spertus JA, Curtis JP, Desai N, Masoudi FA, Bach RG, Mcneely C, Al-Badarin F, House JA, Kulkarni H, Rao SV. The Evolving Landscape of Impella(R) Use in the United States Among Patients Undergoing Percutaneous Coronary Intervention with Mechanical Circulatory Support. *Circulation*.2019;doi:10.1161/CIRCULATIONAHA.119.044007
  62. Hausenloy DJ, Kharbanda RK, Moller UK, Ramlall M, Aaroe J, Butler R, Bulluck H, Clayton T, Dana A, Dodd M, Engstrom T, Evans R, Lassen JF, Christensen EF, Garcia-Ruiz JM, Gorog DA, Hjort J, Houghton RF, Ibanez B, Knight R, Lippert FK, Lonborg JT, Maeng M, Milasinovic D, More R, Nicholas JM, Jensen LO, Perkins A, Radovanovic N, Rakhit RD, Ravkilde J, Ryding AD, Schmidt MR, Riddervold IS, Sorensen HT, Stankovic G, Varma M, Webb I, Terkelsen CJ, Greenwood JP, Yellon DM, Botker HE, Investigators

- C-E-P. Effect of remote ischaemic conditioning on clinical outcomes in patients with acute myocardial infarction (CONDI-2/ERIC-PPCI): a single-blind randomised controlled trial. *Lancet*.2019;394:1415-1424.
63. Waksman R, Di Mario C, Torguson R, Ali ZA, Singh V, Skinner WH, Artis AK, Cate TT, Powers E, Kim C, Regar E, Wong SC, Lewis S, Wykrzykowska J, Dube S, Kazziha S, Van Der Ent M, Shah P, Craig PE, Zou Q, Kolm P, Brewer HB, Garcia-Garcia HM, Investigators LRP. Identification of patients and plaques vulnerable to future coronary events with near-infrared spectroscopy intravascular ultrasound imaging: a prospective, cohort study. *Lancet*.2019;394:1629-1637.
  64. Hong S-J, Mintz GS, Ahn C-M, Kim J-S, Kim B-K, Ko Y-G, Kang T-S, Kang W-C, Kim YH, Hur S-H, Hong B-K, Choi D, Kwon H, Jang Y, Hong M-K, . Effect of Intravascular Ultrasound-Guided Drug-Eluting Stent Implantation: Five-Year Follow-Up of the IVUS-XPL Randomized Trial. *JACC: Cardiovascular Interventions*.2019;
  65. Valgimigli M, Gagnor A, Calabró P, Frigoli E, Leonardi S, Zaro T, Rubartelli P, Briguori C, Andò G, Repetto A, Limbruno U, Cortese B, Sganzerla P, Lupi A, Galli M, Colangelo S, Ierna S, Ausiello A, Presbitero P, Sardella G, Varbella F, Esposito G, Santarelli A, Tresoldi S, Nazzaro M, Zingarelli A, De Cesare N, Rigattieri S, Tosi P, Palmieri C, Brugaletta S, Rao SV, Heg D, Rothenbühler M, Vranckx P, Jüni P. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. *The Lancet*.2015;385:2465-2476.
  66. Nguyen P, Makris A, Hennessy A, Jayanti S, Wang A, Park K, Chen V, Nguyen T, Lo S, Xuan W, Leung M, Juergens C. Standard versus ultrasound-guided radial and femoral access in coronary angiography and intervention (SURF): a randomised controlled trial. *EuroIntervention*.2019;15:e522-e530.
  67. Ali ZA, Nef H, Escaned J, Werner N, Banning AP, Hill JM, De Bruyne B, Montorfano M, Lefevre T, Stone GW, Crowley A, Matsumura M, Maehara A, Lansky AJ, Fajadet J, Di Mario C. Safety and Effectiveness of Coronary Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Stenoses: The Disrupt CAD II Study. *Circ Cardiovasc Interv*.2019;12:e008434.



Table 1 Competition between stents

Trial	Objective	Study	Population	Endpoints	Results	Conclusion	Publication
<b>BIOSTEMI</b>	Ultra-thin strut biodegradable polymer SES (Orsiro) versus thin strut durable-polymer EES (Xience Xpedition) in patients with STEMI	1:1 randomized	1300 patients with STEMI	TLF at 12 months	TLF: RR 0.59 (95% Bayesian CI 0.37-0.94) Posterior probability superiority 0.986 Orsiro:4%; Xience Xpedition:6%;	Orsiro was superior to Xience Xpedition for PCI treatment of STEMI	Iglesias et al. Lancet. 2019
<b>TALENT</b>	Ultra-thin strut biodegradable polymer SES (Supraflex) versus thin strut durable-polymer EES (Xience)	1:1 randomized, non-inferiority study (margin 4.0%)	1436 all-comers patients	TLF at 12 months	TLF: $P_{\text{non-inferiority}} < 0.0001$ Supraflex:4.9%; Xience:5.3%	Supraflex stent was non-inferior compared to Xience stent	Zaman et al. Lancet 2019;393:987-97
<b>SORT-OUT VIII</b>	Thin-strut biodegradable polymer EES (Synergy) versus biodegradable polymer BES (BioMatrix NeoFlex)	1:1 randomized, non-inferiority trial (margin of 3.0%)	2764 all-comers patients	TLF at 12 months	TLF: $P_{\text{non-inferiority}} < 0.001$ Synergy 4.0%; BioMatrix NeoFlex 4.4%	BioMatrix NeoFlex was non-inferior to Synergy	Maeng et al. J Am Coll Cardiol Intv. 2019;12:624-33
<b>MASTER</b>	Biodegradable polymer SES (Ultimaster) versus a BMS (Kaname bare metal) for the treatment of STEMI	3:1 randomized (BP-SES 375 pts vs BMS 125 pts) non-inferiority trial (margin 3.0%)	500 patients undergoing primary PCI for STEMI	TVF at 12 months	TVF: $P_{\text{non-inferiority}} = 0.0004$ Ultimaster stent: 6.1%; Kaname bare metal stent: 14.4%	Ultimaster was clinically non-inferior to Kaname BMS for PCI treatment of STEMI	Valdes-Chavarri et al. EuroIntervention. 2019;14:e1836-42
<b>ReCre8</b>	Polymer-free AES (Cre8) versus permanent-polymer ZES (Resolute Integrity)	1:1 randomized, physician-initiated, non-inferiority trial (margin 3.5%)	1502 all-comers patients	TLF at 12 months	TLF: $P_{\text{non-inferiority}} = 0.0086$ Cre8: 6.2%; Resolute Integrity:5.6%	Cre8 was non-inferior to Resolute Integrity	Rozemeijer et al. Circulation. 2019;139:67-77

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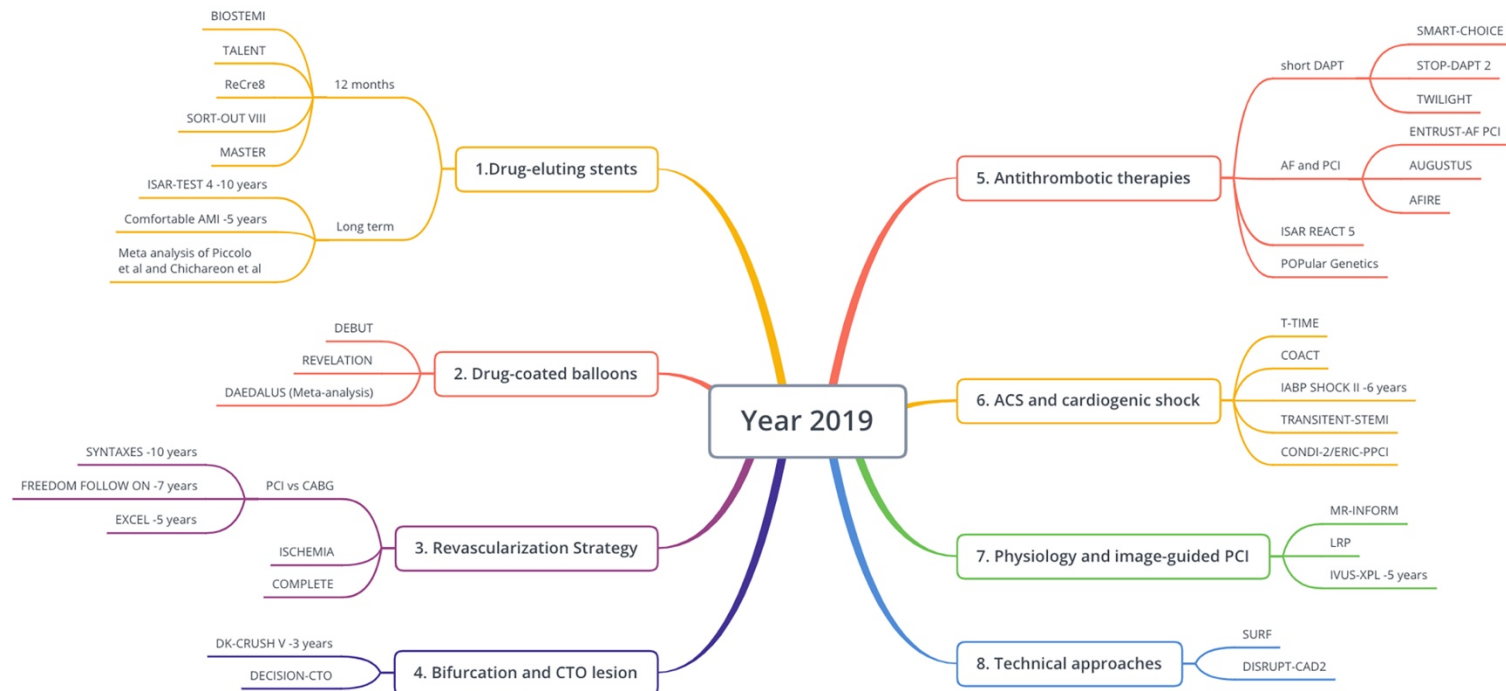
<b>BIOFLOW-IV</b>	Ultra-thin strut biodegradable polymer SES (Orsiro) versus thin strut durable-polymer EES (Xience Xpedition) in patients with STEMI	1:1 randomized	575 all-comers patients	TVF at 12 months	TVF: P <sub>non-inferiority</sub> <0.001 Orsiro:5.5%; Xience Xpedition:7.5%;	Orsiro was non-inferior to Xience Xpedition	Saito et al. EuroIntervention 2019;15:e1006-e1013
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EES: Everolimus-eluting stent; SES: Sirolimus-eluting stent; BES: Biolimus-eluting stent; BMS: Bare-metal stent; AES: Amphilimus-eluting stents;

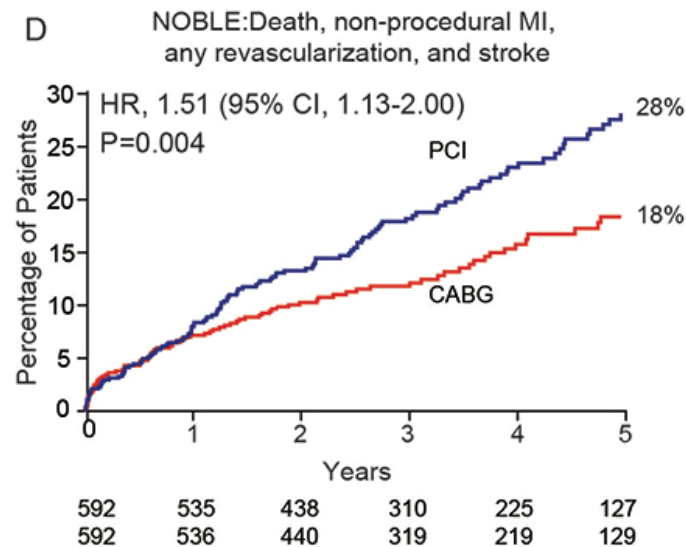
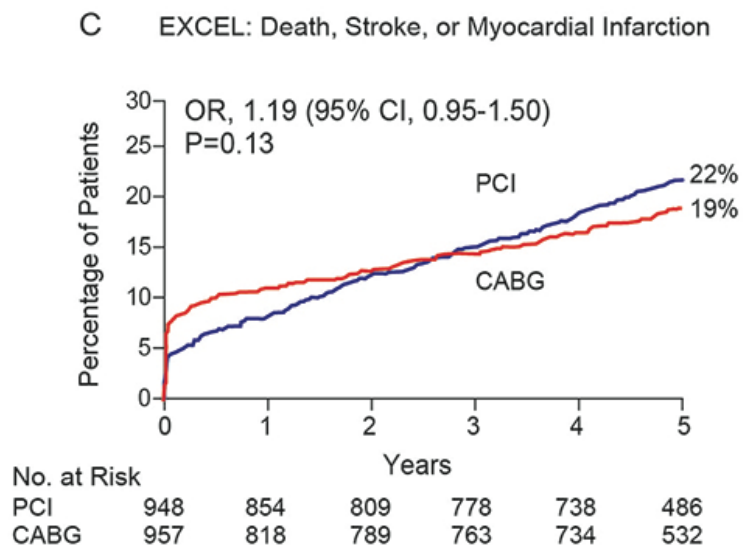
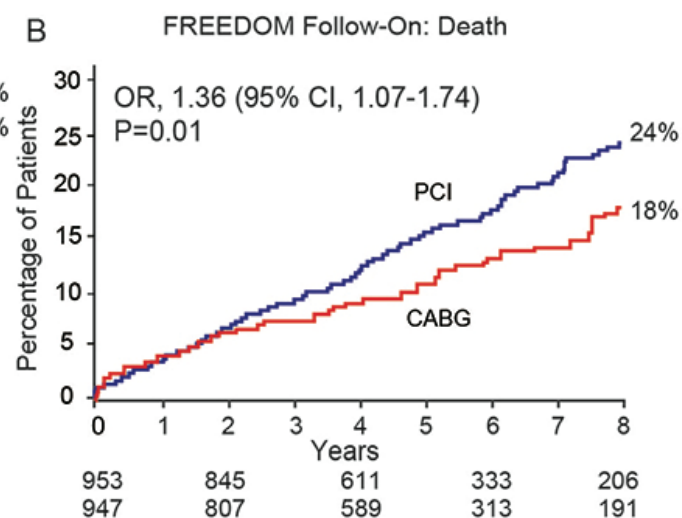
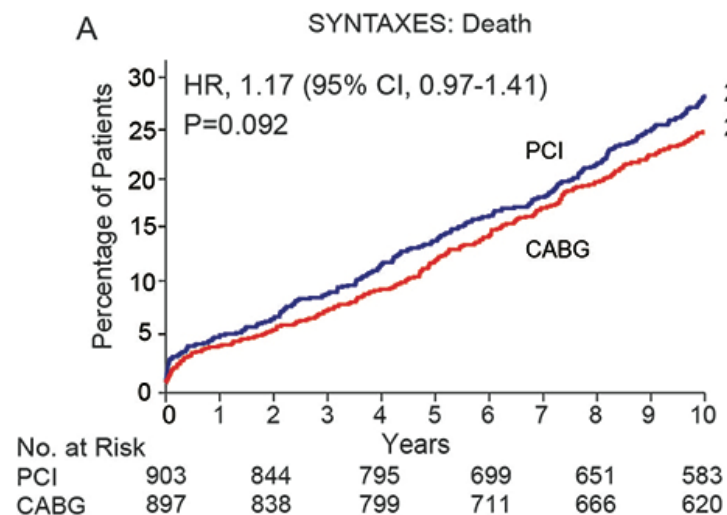
ZES: Zotarolimus-eluting stents; TLF: Target lesion failure, defined as cardiac death, target-vessel MI, clinical indicated target lesion

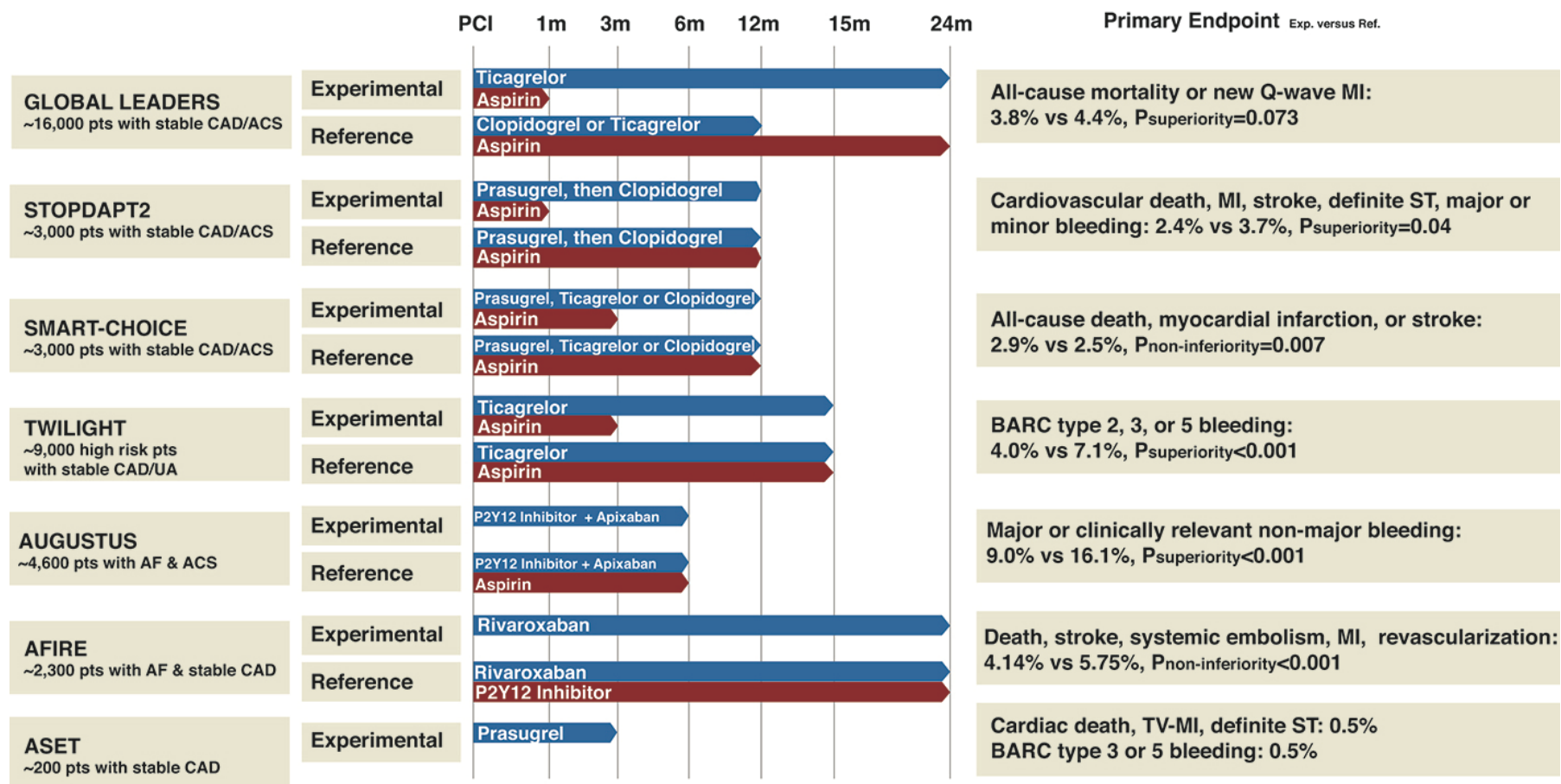
revascularization; TVF: Target vessel failure, defined as cardiac death, MI or clinically driven target vessel revascularization

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