Supplement to
Cardiology today

AUGUST 2015

STEMI Treatment Focus: PCI

Recent headlines examine this multifaceted treatment approach

PRAGUE 13

Multivessel PCI fails to best culprit-vessel PCI after STEMI

TOTAL

Stroke risk associated with manual thrombectomy evident within 48 hours

CathPCI Registry-CMS dataset

Shorter hospital stay safe for older patients with STEMI

Single-center STEMI registry

No evidence of 'smoker's paradox' found

DANAMI3-PRIMULTI

Complete revascularization benefits patients with multivessel CAD requiring PCI

This CARDIOLOGY TODAY supplement is produced by SLACK Incorporated.

NO ONE WANTS A REMATCH AGAINST STEMI.

See why Effient may be appropriate for your STEMI-PCI patients at high risk for a second thrombotic CV event at EffientHCP.com.

Effient® (prasugrel) is indicated to reduce the rate of thrombotic cardiovascular (CV) events (including stent thrombosis) in patients with acute coronary syndrome (ACS) who are to be managed with percutaneous coronary intervention (PCI) as follows: [1] patients with unstable angina (UA) or non–ST-elevation myocardial infarction (NSTEMI); [2] patients with ST-elevation myocardial infarction (STEMI) when managed with primary or delayed PCI.

The loading dose (LD) of Effient is 60 mg and the maintenance dose (MD) is 10 mg once daily. Effient is available in 5-mg and 10-mg tablets.

IMPORTANT SAFETY INFORMATION

WARNING: BLEEDING RISK

Effient® (prasugrel) can cause significant, sometimes fatal, bleeding.

Do not use Effient in patients with active pathological bleeding or a history of transient ischemic attack or stroke.

In patients ≥75 years of age, Effient is generally not recommended, because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior myocardial infarction [MI]) where its effect appears to be greater and its use may be considered.

Do not start Effient in patients likely to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue Effient at least 7 days prior to any surgery.

Additional risk factors for bleeding include:

- body weight <60 kg
- propensity to bleed
- concomitant use of medications that increase the risk of bleeding (eg, warfarin, heparin, fibrinolytic therapy, chronic use of nonsteroidal anti-inflammatory drugs [NSAIDs])

Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of Effient.

If possible, manage bleeding without discontinuing Effient. Discontinuing Effient, particularly in the first few weeks after acute coronary syndrome, increases the risk of subsequent cardiovascular events.

CONTRAINDICATIONS

- Effient is contraindicated in patients with active pathological bleeding, such as from a peptic ulcer or intracranial hemorrhage (ICH), or a history of transient ischemic attack (TIA) or stroke, and in patients with hypersensitivity to prasugrel or any component of the product

WARNINGS AND PRECAUTIONS

- Patients who experience a stroke or TIA while on Effient generally should have therapy discontinued. Effient should also be discontinued for active bleeding and elective surgery
- Premature discontinuation of Effient increases risk of stent thrombosis, MI, and death
- Thrombotic thrombocytopenic purpura (TTP), a rare but serious condition that can be fatal, has been reported with Effient, sometimes after a brief exposure (<2 weeks), and requires urgent treatment, including plasmapheresis
- Hypersensitivity, including angioedema, has been reported in patients receiving Effient, including patients with a history of hypersensitivity reaction to other thienopyridines

ADVERSE REACTIONS

- Bleeding, including life-threatening and fatal bleeding, is the most commonly reported adverse reaction

Please see Brief Summary of Prescribing Information, including Boxed Warning regarding bleeding risk, on subsequent pages.

Daiichi-Sankyo Lilly

PGHCPISI03Oct2011 PG97598.

Effient® (prasugrel) tablets

Effient® (prasugrel) tablets
Brief Summary of Prescribing Information

BRIEF SUMMARY: Please see Full Prescribing Information for additional information about Effient.

WARNING: BLEEDING RISK

- **Effient can cause significant, sometimes fatal, bleeding *[see Warnings and Precautions (5.1, 5.2) and Adverse Reactions (6.1)]*.**
- **Do not use Effient in patients with active pathological bleeding or a history of transient ischemic attack or stroke *[see Contraindications (4.1, 4.2)]*.**
- **In patients ≥75 years of age, Effient is generally not recommended, because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior MI) where its effect appears to be greater and its use may be considered *[see Use in Specific Populations (8.5)]*.**
- **Do not start Effient in patients likely to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue Effient at least 7 days prior to any surgery *[see Warnings and Precautions (5.2)]*.**
- **Additional risk factors for bleeding include: body weight <60 kg; propensity to bleed; concomitant use of medications that increase the risk of bleeding (e.g., warfarin, heparin, fibrinolytic therapy, chronic use of non-steroidal anti-inflammatory drugs [NSAIDs]) *[see Warnings and Precautions (5.1)]*.**
- **Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of Effient *[see Warnings and Precautions (5.1)]*.**
- **If possible, manage bleeding without discontinuing Effient. Discontinuing Effient, particularly in the first few weeks after acute coronary syndrome, increases the risk of subsequent cardiovascular events *[see Warnings and Precautions (5.3)]*.**

1 INDICATIONS AND USAGE

1.1 Acute Coronary Syndrome: Effient® is indicated to reduce the rate of thrombotic cardiovascular (CV) events (including stent thrombosis) in patients with acute coronary syndrome (ACS) who are to be managed with percutaneous coronary intervention (PCI) as follows:

- Patients with unstable angina (UA) or non–ST-elevation myocardial infarction (NSTEMI).
- Patients with ST-elevation myocardial infarction (STEMI) when managed with primary or delayed PCI.

Effient has been shown to reduce the rate of a combined endpoint of cardiovascular death, nonfatal myocardial infarction (MI), or nonfatal stroke compared to clopidogrel. The difference between treatments was driven predominantly by MI, with no difference on strokes and little difference on CV death *[see Clinical Studies (14)]*.

It is generally recommended that antiplatelet therapy be administered promptly in the management of ACS because many cardiovascular events occur within hours of initial presentation. In the clinical trial that established the efficacy of Effient, Effient and the control drug were not administered to UA/NSTEMI patients until coronary anatomy was established. For the small fraction of patients that required urgent CABG after treatment with Effient, the risk of significant bleeding was substantial *[see Warnings and Precautions (5.2)]*. Because the large majority of patients are managed without CABG, however, treatment can be considered before determining coronary anatomy if need for CABG is considered unlikely. The advantages of earlier treatment with Effient must then be balanced against the increased rate of bleeding in patients who do need to undergo urgent CABG.

2 DOSAGE AND ADMINISTRATION

Initiate Effient treatment as a single 60-mg oral loading dose and then continue at 10-mg orally once daily. Patients taking Effient should also take aspirin (75-mg to 325-mg) daily *[see Drug Interactions (7.3) and Clinical Pharmacology (12.3)]*. Effient may be administered with or without food *[see Clinical Pharmacology (12.3) and Clinical Studies (14)]*.

Dosing in Low Weight Patients: Compared to patients weighing ≥60 kg, patients weighing <60 kg have an increased exposure to the active metabolite of prasugrel and an increased risk of bleeding on a 10-mg once daily maintenance dose. Consider lowering the maintenance dose to 5-mg in patients <60 kg. The effectiveness and safety of the 5-mg dose have not been prospectively studied *[see Warnings and Precautions (5.1), Adverse Reactions (6.1), and Clinical Pharmacology (12.3)]*.

4 CONTRAINDICATIONS

4.1 Active Bleeding: Effient is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*.

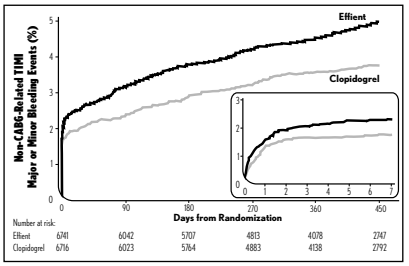
4.2 Prior Transient Ischemic Attack or Stroke: Effient is contraindicated in patients with a history of prior transient ischemic attack (TIA) or stroke. In TRITON-TIMI 38 (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel), patients with a history of TIA or ischemic stroke (>3 months prior to enrollment) had a higher rate of stroke on Effient (6.5%; of which 4.2% were thrombotic stroke and 2.3% were intracranial hemorrhage [ICH]) than on clopidogrel (1.2%; all thrombotic). In patients without such a history, the incidence of stroke was 0.9% (0.2% ICH) and 1.0% (0.3% ICH) with Effient and clopidogrel, respectively. Patients with a history of ischemic stroke within 3 months of screening and patients with a history of hemorrhagic stroke at any time were excluded from TRITON-TIMI 38. Patients who experience a stroke or TIA while on Effient generally should have therapy discontinued *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

4.3 Hypersensitivity: Effient is contraindicated in patients with hypersensitivity (e.g., anaphylaxis) to prasugrel or any component of the product *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 General Risk of Bleeding: Thienopyridines, including Effient, increase the risk of bleeding. With the dosing regimens used in TRITON-TIMI 38, TIMI (Thrombolysis in Myocardial Infarction) Major (clinically overt bleeding associated with a fall in hemoglobin ≥5 g/dL, or intracranial hemorrhage) and TIMI Minor (overt bleeding associated with a fall in hemoglobin of ≥3 g/dL but <5 g/dL) bleeding events were more common on Effient than on clopidogrel *[see Adverse Reactions (6.1)]*. The bleeding risk is highest initially, as shown in Figure 1 (events through 450 days; inset shows events through 7 days).

Figure 1: Non-CABG-Related TIMI Major or Minor Bleeding Events.



Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, PCI, CABG, or other surgical procedures even if the patient does not have overt signs of bleeding. Do not use Effient in patients with active bleeding, prior TIA or stroke *[see Contraindications (4.1, 4.2)]*.

Other risk factors for bleeding are:

- Age ≥75 years. Because of the risk of bleeding (including fatal bleeding) and uncertain effectiveness in patients ≥75 years of age, use of Effient is generally not recommended in these patients, except in high-risk situations (patients with diabetes or history of myocardial infarction) where its effect appears to be greater and its use may be considered *[see Adverse Reactions (6.1), Use in Specific Populations (8.5), Clinical Pharmacology (12.3), and Clinical Trials (14)]*.
- CABG or other surgical procedure *[see Warnings and Precautions (5.2)]*.
- Body weight <60 kg. Consider a lower (5-mg) maintenance dose *[see Dosage and Administration (2), Adverse Reactions (6.1), and Use in Specific Populations (8.6)]*.
- Propensity to bleed (e.g., recent trauma, recent surgery, recent or recurrent gastrointestinal (GI) bleeding, active peptic ulcer disease, or severe hepatic impairment) *[see Adverse Reactions (6.1) and Use in Specific Populations (8.7, 8.8)]*.
- Medications that increase the risk of bleeding (e.g., oral anticoagulants, chronic use of non-steroidal anti-inflammatory drugs [NSAIDs], and fibrinolytic agents). Aspirin and heparin were commonly used in TRITON-TIMI 38 *[see Drug Interactions (7.1, 7.2, 7.3), and Clinical Studies (14)]*.

Thienopyridines inhibit platelet aggregation for the lifetime of the platelet (7-10 days), so withholding a dose will not be useful in managing a bleeding event or the risk of bleeding associated with an invasive procedure. Because the half-life of prasugrel's active metabolite is short relative to the lifetime of the platelet, it may be possible to restore hemostasis by administering exogenous platelets; however, platelet transfusions within 6 hours of the loading dose or 4 hours of the maintenance dose may be less effective.

5.2 Coronary Artery Bypass Graft Surgery-Related Bleeding: The risk of bleeding is increased in patients receiving Effient who undergo CABG. If possible, Effient should be discontinued at least 7 days prior to CABG.

Of the 437 patients who underwent CABG during TRITON-TIMI 38, the rates of CABG-related TIMI Major or Minor bleeding were 14.1% in the Effient group and 4.5% in the clopidogrel group *[see Adverse Reactions (6.1)]*. The higher risk for bleeding events in patients treated with Effient persisted up to 7 days from the most recent dose of study drug. For patients receiving a thienopyridine within 3 days prior to CABG, the frequencies of TIMI Major or Minor bleeding were 26.7% (12 of 45 patients) in the Effient group, compared with 5.0% (3 of 60 patients) in the clopidogrel group. For patients who received their last dose of thienopyridine within 4 to 7 days prior to CABG, the frequencies decreased to 11.3% (9 of 80 patients) in the prasugrel group and 3.4% (3 of 89 patients) in the clopidogrel group.

Do not start Effient in patients likely to undergo urgent CABG. CABG-related bleeding may be treated with transfusion of blood products, including packed red blood cells and platelets; however, platelet transfusions within 6 hours of the loading dose or 4 hours of the maintenance dose may be less effective.

5.3 Discontinuation of Effient: Discontinue thienopyridines, including Effient, for active bleeding, elective surgery, stroke, or TIA. The optimal duration of thienopyridine therapy is unknown. In patients who are managed with PCI and stent placement, premature discontinuation of any antiplatelet medication, including thienopyridines, conveys an increased risk of stent thrombosis, myocardial infarction, and death. Patients who require premature discontinuation of a thienopyridine will be at increased risk for cardiac events. Lapses in therapy should be avoided, and if thienopyridines must be temporarily discontinued because of an adverse event(s), they should be restarted as soon as possible *[see Contraindications (4.1, 4.2) and Warnings and Precautions (5.1)]*.

5.4 Thrombotic Thrombocytopenic Purpura: Thrombotic thrombocytopenic purpura (TTP) has been reported with the use of Effient. TTP can occur after a brief exposure (<2 weeks). TTP is a serious condition that can be fatal and requires urgent treatment, including plasmapheresis (plasma exchange). TTP is characterized by thrombocytopenia, microangiopathic hemolytic anemia (schistocytes [fragment red blood cells] seen on peripheral smear), neurological findings, renal dysfunction, and fever *[see Adverse Reactions (6.2)]*.

5.5 Hypersensitivity Including Angioedema: Hypersensitivity including angioedema has been reported in patients receiving Effient, including patients with a history of hypersensitivity reaction to other thienopyridines *[see Contraindications (4.3) and Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience: The following serious adverse reactions are also discussed elsewhere in the labeling:

- Bleeding *[see Boxed Warning and Warnings and Precautions (5.1, 5.2)]*
- Thrombotic thrombocytopenic purpura *[see Warnings and Precautions (5.4)]*

Safety in patients with ACS undergoing PCI was evaluated in a clopidogrel-controlled study, TRITON-TIMI 38, in which 6741 patients were treated with Effient (60-mg loading dose and 10-mg once daily) for a median of 14.5 months (5802 patients were treated for over 6 months; 4136 patients were treated for more than 1 year). The population treated with Effient was 27 to 96 years of age, 25% female, and 92% Caucasian. All patients in the TRITON-TIMI 38 study were to receive aspirin. The dose of clopidogrel in this study was a 300-mg loading dose and 75-mg once daily.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials cannot be directly compared with the rates observed in other clinical trials of another drug and may not reflect the rates observed in practice.

Drug Discontinuation: The rate of study drug discontinuation because of adverse reactions was 7.2% for Effient and 6.3% for clopidogrel. Bleeding was the most common adverse reaction leading to study drug discontinuation for both drugs (2.5% for Effient and 1.4% for clopidogrel).

Bleeding: *Bleeding Unrelated to CABG Surgery* - In TRITON-TIMI 38, overall rates of TIMI Major or Minor bleeding adverse reactions unrelated to coronary artery bypass graft surgery (CABG) were significantly higher on Effient than on clopidogrel, as shown in Table 1.

Table 1: Non-CABG-Related Bleeding[a] (TRITON-TIMI 38)

	Effient (%) (N=6741)	Clopidogrel (%) (N=6716)
TIMI Major or Minor bleeding	4.5	3.4
TIMI Major bleeding[b]	2.2	1.7
Life-threatening	1.3	0.8
Fatal	0.3	0.1
Symptomatic intracranial hemorrhage (ICH)	0.3	0.3
Requiring inotropes	0.3	0.1
Requiring surgical intervention	0.3	0.3
Requiring transfusion (≥4 units)	0.7	0.5
TIMI Minor bleeding[b]	2.4	1.9

[a]Patients may be counted in more than one row.
[b]See 5.1 for definition.

Figure 1 demonstrates non-CABG related TIMI Major or Minor bleeding. The bleeding rate is highest initially, as shown in Figure 1 (inset: Days 0 to 7) *[see Warnings and Precautions (5.1)]*.

Bleeding by Weight and Age - In TRITON-TIMI 38, non-CABG-related TIMI Major or Minor bleeding rates in patients with the risk factors of age ≥75 years and weight <60 kg are shown in Table 2.

Table 2: Bleeding Rates for Non-CABG-Related Bleeding by Weight and Age (TRITON-TIMI 38)

	Major/Minor		Fatal	
	Effient[a] (%)	Clopidogrel[b] (%)	Effient[a] (%)	Clopidogrel[b] (%)
Weight <60 kg (N=308 Effient, N=356 clopidogrel)	10.1	6.5	0.0	0.3
Weight ≥60 kg (N=6373 Effient, N=6299 clopidogrel)	4.2	3.3	0.3	0.1
Age <75 years (N=5850 Effient, N=5822 clopidogrel)	3.8	2.9	0.2	0.1
Age ≥75 years (N=891 Effient, N=894 clopidogrel)	9.0	6.9	1.0	0.1

[a]10-mg Effient maintenance dose.

[b]75-mg clopidogrel maintenance dose.

Bleeding Related to CABG - In TRITON-TIMI 38, 437 patients who received a thienopyridine underwent CABG during the course of the study. The rate of CABG-related TIMI Major or Minor bleeding was 14.1% for the Effient group and 4.5% in the clopidogrel group (*see* Table 3). The higher risk for bleeding adverse reactions in patients treated with Effient persisted up to 7 days from the most recent dose of study drug.

Table 3: CABG-Related Bleeding[a] (TRITON-TIMI 38)

	Effient (%) (N=213)	Clopidogrel (%) (N=224)
TIMI Major or Minor bleeding	14.1	4.5
TIMI Major bleeding	11.3	3.6
Fatal	0.9	0
Reoperation	3.8	0.5
Transfusion of ≥5 units	6.6	2.2
Intracranial hemorrhage	0	0
TIMI Minor bleeding	2.8	0.9

[a]Patients may be counted in more than one row.

Bleeding Reported as Adverse Reactions - Hemorrhagic events reported as adverse reactions in TRITON-TIMI 38 were, for Effient and clopidogrel, respectively: epistaxis (6.2%, 3.3%), gastrointestinal hemorrhage (1.5%, 1.0%), hemoptysis (0.6%, 0.5%), subcutaneous hematoma (0.5%, 0.2%), post-procedural hemorrhage (0.5%, 0.2%), retroperitoneal hemorrhage (0.3%, 0.2%), pericardial effusion/hemorrhage/tamponade (0.3%, 0.2%), and retinal hemorrhage (0.0%, 0.1%).

Malignancies: During TRITON-TIMI 38, newly-diagnosed malignancies were reported in 1.6% and 1.2% of patients treated with prasugrel and clopidogrel, respectively. The sites contributing to the differences were primarily colon and lung. In another Phase 3 clinical study of ACS patients not undergoing PCI, in which data for malignancies were prospectively collected, newly-diagnosed malignancies were reported in 1.8% and 1.7% of patients treated with prasugrel and clopidogrel, respectively. The site of malignancies was balanced between treatment groups except for colorectal malignancies. The rates of colorectal malignancies were 0.3% prasugrel, 0.1% clopidogrel and most were detected during investigation of GI bleed or anemia. It is unclear if these observations are causally-related, are the result of increased detection because of bleeding, or are random occurrences.

Other Adverse Events: In TRITON-TIMI 38, common and other important non-hemorrhagic adverse events were, for Effient and clopidogrel, respectively: severe thrombocytopenia (0.06%, 0.04%), anemia (2.2%, 2.0%), abnormal hepatic function (0.22%, 0.27%), allergic reactions (0.36%, 0.36%), and angioedema (0.06%, 0.04%). Table 4 summarizes the adverse events reported by at least 2.5% of patients.

Table 4: Non-Hemorrhagic Treatment Emergent Adverse Events Reported by at Least 2.5% of Patients in Either Group

	Effient (%) (N=6741)	Clopidogrel (%) (N=6716)
Hypertension	7.5	7.1
Hypercholesterolemia/Hyperlipidemia	7.0	7.4
Headache	5.5	5.3
Back pain	5.0	4.5
Dyspnea	4.9	4.5
Nausea	4.6	4.3
Dizziness	4.1	4.6
Cough	3.9	4.1
Hypotension	3.9	3.8
Fatigue	3.7	4.8
Non-cardiac chest pain	3.1	3.5
Atrial fibrillation	2.9	3.1
Bradycardia	2.9	2.4
Leukopenia (<4 x 10^3 WBC/L)	2.8	3.5
Rash	2.8	2.4
Pyrexia	2.7	2.2
Peripheral edema	2.7	3.0
Pain in extremity	2.6	2.6
Diarrhea	2.3	2.6

6.2 Postmarketing Experience: The following adverse reactions have been identified during post approval use of Effient. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and lymphatic system disorders — Thrombocytopenia, Thrombotic thrombocytopenic purpura (TTP) *[see Warnings and Precautions (5.4) and Patient Counseling Information (17)]*

Immune system disorders — Hypersensitivity reactions including anaphylaxis *[see Contraindications (4.3)]*

7 DRUG INTERACTIONS

7.1 Warfarin: Coadministration of Effient and warfarin increases the risk of bleeding *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

7.2 Non-Steroidal Anti-Inflammatory Drugs: Coadministration of Effient and NSAIDs (used chronically) may increase the risk of bleeding *[see Warnings and Precautions (5.1)]*.

7.3 Other Concomitant Medications: Effient can be administered with drugs that are inducers or inhibitors of cytochrome P450 enzymes *[see Clinical Pharmacology (12.3)]*.

Effient can be administered with aspirin (75-mg to 325-mg per day), heparin, GPIIb/IIIa inhibitors, statins, digoxin, and drugs that elevate gastric pH, including proton pump inhibitors and H_2 blockers *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: *Pregnancy Category B* - There are no adequate and well-controlled studies of Effient use in pregnant women. Reproductive and developmental toxicology studies in rats and rabbits at doses of up to 30 times the recommended therapeutic exposures in humans (based on plasma exposures to the major circulating human metabolite) revealed no evidence of fetal harm; however, animal studies are not always predictive of a human response. Effient should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

In embryo fetal developmental toxicology studies, pregnant rats and rabbits received prasugrel at maternally toxic oral doses equivalent to more than 40 times the human exposure. A slight decrease in pup body weight was observed; but, there were no structural malformations in either species. In prenatal and postnatal rat studies, maternal treatment with prasugrel had no effect on the behavioral or reproductive development of the offspring at doses greater than 150 times the human exposure *[see Nonclinical Toxicology (13.1)]*.

8.3 Nursing Mothers: It is not known whether Effient is excreted in human milk; however, metabolites of Effient were found in rat milk. Because many drugs are excreted in human milk, prasugrel should be used during nursing only if the potential benefit to the mother justifies the potential risk to the nursing infant.

8.4 Pediatric Use: Safety and effectiveness in pediatric patients have not been established *[see Clinical Pharmacology (12.3)]*.

8.5 Geriatric Use: In TRITON-TIMI 38, 38.5% of patients were ≥65 years of age and 13.2% were ≥75 years of age. The risk of bleeding increased with advancing age in both treatment groups, although the relative risk of bleeding (Effient compared with clopidogrel) was similar across age groups.

Patients ≥75 years of age who received Effient 10-mg had an increased risk of fatal bleeding events (1.0%) compared to patients who received clopidogrel (0.1%). In patients ≥75 years of age, symptomatic intracranial hemorrhage occurred in 7 patients (0.8%) who received Effient and in 3 patients (0.3%) who received clopidogrel. Because of the risk of bleeding, and because effectiveness is uncertain in patients ≥75 years of age *[see Clinical Studies (14)]*, use of Effient is generally not recommended in these patients, except in high-risk situations (diabetes and past history of myocardial infarction) where its effect appears to be greater and its use may be considered *[see Warnings and Precautions (5.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*.

8.6 Low Body Weight: In TRITON-TIMI 38, 4.6% of patients treated with Effient had body weight <60 kg. Individuals with body weight <60 kg had an increased risk of bleeding and an increased exposure to the active metabolite of prasugrel *[see Dosage and Administration (2), Warnings and Precautions (5.1), and Clinical Pharmacology (12.3)]*. Consider lowering the maintenance dose to 5-mg in patients <60 kg. The effectiveness and safety of the 5-mg dose have not been prospectively studied *[see Dosage and Administration (2) and Clinical Pharmacology (12.3)]*.

8.7 Renal Impairment: No dosage adjustment is necessary for patients with renal impairment. There is limited experience in patients with end-stage renal disease, but such patients are generally at higher risk of bleeding *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

8.8 Hepatic Impairment: No dosage adjustment is necessary in patients with mild to moderate hepatic impairment (Child-Pugh Class A and B). The pharmacokinetics and pharmacodynamics of prasugrel in patients with severe hepatic disease have not been studied, but such patients are generally at higher risk of bleeding *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

8.9 Metabolic Status: In healthy subjects, patients with stable atherosclerosis, and patients with ACS receiving prasugrel, there was no relevant effect of genetic variation in CYP2B6, CYP2C9, CYP2C19, or CYP3A5 on the pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation.

10 OVERDOSAGE

10.1 Signs and Symptoms: Platelet inhibition by prasugrel is rapid and irreversible, lasting for the life of the platelet, and is unlikely to be increased in the event of an overdose. In rats, lethality was observed after administration of 2000 mg/kg. Symptoms of acute toxicity in dogs included emesis, increased serum alkaline phosphatase, and hepatocellular atrophy. Symptoms of acute toxicity in rats included mydriasis, irregular respiration, decreased locomotor activity, ptosis, staggering gait, and lacrimation.

10.2 Recommendations about Specific Treatment: Platelet transfusion may restore clotting ability. The prasugrel active metabolite is not likely to be removed by dialysis.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility: *Carcinogenesis* - No compound-related tumors were observed in a 2-year rat study with prasugrel at oral doses up to 100 mg/kg/day (>100 times the recommended therapeutic exposures in humans (based on plasma exposures to the major circulating human metabolite). There was an increased incidence of tumors (hepatocellular adenomas) in mice exposed for 2 years to high doses (>250 times the human metabolite exposure).

Mutagenesis - Prasugrel was not genotoxic in two *in vitro* tests (Ames bacterial gene mutation test, clastogenicity assay in Chinese hamster fibroblasts) and in one *in vivo* test (micronucleus test by intraperitoneal route in mice).

Impairment of Fertility - Prasugrel had no effect on fertility of male and female rats at oral doses up to 300 mg/kg/day (80 times the human major metabolite exposure at daily dose of 10-mg prasugrel).

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide)

Benefits and Risks

- Summarize the effectiveness features and potential side effects of Effient.
- Tell patients to take Effient exactly as prescribed.
- Remind patients not to discontinue Effient without first discussing it with the physician who prescribed Effient.
- Recommend that patients read the Medication Guide.

Bleeding: Inform patients that they:

- will bruise and bleed more easily.
- will take longer than usual to stop bleeding.
- should report any unanticipated, prolonged, or excessive bleeding, or blood in their stool or urine.

Other Signs and Symptoms Requiring Medical Attention

- Inform patients that TTP is a rare but serious condition that has been reported with Effient.
  - Instruct patients to get prompt medical attention if they experience any of the following symptoms that cannot otherwise be explained: fever, weakness, extreme skin paleness, purple skin patches, yellowing of the skin or eyes, or neurological changes.
- Inform patients that they may have hypersensitivity reactions including rash, angioedema, anaphylaxis, or other manifestations. Patients who have had hypersensitivity reactions to other thienopyridines may have hypersensitivity reactions to Effient.

Invasive Procedures: Instruct patients to:

- inform physicians and dentists that they are taking Effient before any invasive procedure is scheduled.
- tell the doctor performing the invasive procedure to talk to the prescribing health care professional before stopping Effient.

Concomitant Medications: Ask patients to list all prescription medications, over-the-counter medications, or dietary supplements they are taking or plan to take so the physician knows about other treatments that may affect bleeding risk (e.g., warfarin and NSAIDs).

Effient® is a registered trademark of Eli Lilly and Company.

Manufactured by Eli Lilly and Company, Indianapolis, IN 46285

Marketed by Daiichi Sankyo, Inc. and Lilly USA, LLC

PG88009. PGHCPBS15Nov2013.

PCI in the treatment of STEMI:
Quest for best treatment regimen continues

Despite varied approaches to antithrombotic therapy, shifts in reperfusion strategies including the introduction of primary PCI, and developments in coordinated care, STEMI remains a major cause of death and disability around the globe.

The cardiology community is keen to uncover optimum treatment regimens and untangle dilemmas surrounding PCI to improve CV outcomes and further decrease STEMI mortality rates, still lingering at 5% to 6% in hospital and at 7% to 18% at 1 year, according to recent data.

This supplement, brought to you by the editors of CARDIOLOGY TODAY, offers the latest knowledge on managing STEMI with PCI through results revealed at the ACC Scientific Sessions in San Diego and the EuroPCR congress of the European Association of Percutaneous Cardiovascular Interventions in Paris, as well as published findings.

Readers will gather key clinical takeaways on multivessel vs. culprit-only primary PCI from the PRAGUE 13 trial and on stroke risk with manual thrombectomy during PCI from the TOTAL trial, with additional results on timing, severity, subtypes and predictors.

With an analysis of the CathPCI Resigstry-CMS dataset demonstrating differences in clinical outcomes in older patients by duration of hospital stay and the DANAMI3-PRIMULTI study showing revascularization benefits in patients with CAD, this resource provides physicians with information that directly impacts everyday practice.

For additional headlines on the treatment of patients with STEMI, visit Healio.com/Cardiology. ■

– *The Publisher of* CARDIOLOGY TODAY

WEB WATCH

Healio.com | Cardiology today

SCAI special lecture looks ahead at clinical research in interventional cardiology

VIDEO COVERAGE

Robert A. Harrington, MD, FACC, FAHA, FESC, professor of medicine and chairman of the department of medicine at Stanford University, outlines five possible avenues to improve clinical research and underscores the importance of public funding and the health benefits that follow NIH investment and biomedical research. See this video and more at Healio.com/SCAIVideos.

Find daily coverage at **Healio.com/Cardiology**

Cardiology today's Intervention

Find coverage of compelling research in interventional cardiology with in-depth clinical perspectives from leading experts in the latest CARDIOLOGY TODAY'S INTERVENTION print issue, now online. This month's cover story explores acute stroke as a new target for endovascular therapy.

SLACK INCORPORATED *Delivering the best in health care information and education worldwide*

6900 Grove Road, Thorofare, NJ 08086 USA • phone: 856-848-1000 • Healio.com/Cardiology
This CARDIOLOGY TODAY supplement is produced by SLACK Incorporated.

Originally posted on Healio.com/Cardiology | May 29, 2015

PRAGUE 13: Multivessel PCI fails to best culprit-vessel PCI after STEMI

New data from the PRAGUE 13 trial presented at EuroPCR demonstrate no difference in favor of multivessel PCI over culprit-only primary PCI in patients with STEMI.

Ota Hlinomaz, MD, PhD, from St. Anne University Hospital in Brno, Czech Republic, and colleagues studied two management strategies in patients with STEMI who had 70% or greater stenosis in a nonculprit artery.

The study included 106 patients who underwent complete revascularization of all significant stenoses in noninfarct coronary arteries — which Hlinomaz said involved a staged PCI performed from day 3 to 40 after intervention — and 108 patients who received conservative management based on guideline-recommended treatment.

Ota Hlinomaz

The primary composite endpoint included all-cause death, nonfatal MI and stroke, which occurred in 16% of patients in the multivessel PCI group vs. 13.9% in the conservative therapy group (HR = 1.35; 95% CI, 0.66-2.74). The all-cause mortality rate was 5.7% for the multivessel PCI group vs. 6.5% for the conservative therapy group (HR = 0.91; 95% CI, 0.30-2.70), the rate of nonfatal MI was 10.4% vs. 7.4%, respectively (HR = 1.71; 95% CI, 0.66-4.41) and the rate of stroke was 0% vs. 2.8%, respectively. Hlinomaz also reported that 3.8% of patients in the multivessel PCI group had periprocedural infarctions with good prognoses.

All-cause mortality rate

5.7%	6.5%
Multivessel PCI	Conservative Therapy

Other results indicated no significant difference between the two groups in hospitalization for unstable angina (P = .193) or hospitalization for HF (P = .672), CV mortality (P = .699) and revascularization for a noninfarct artery (P = .089).

"This trial found no difference, not even a trend, favoring staged multivessel PCI over culprit-only primary PCI in STEMI," Hlinomaz said during a presentation. "Larger trials are needed to clarify the revascularization strategy in STEMI patients with multivessel disease." – *by Rob Volansky*

Reference:
Hlinomaz O, et al. Hot Line: Late-Breaking Trials and Innovations. Presented at: EuroPCR; May 19-22, 2015; Paris.

Disclosure: Hlinomaz reports no relevant financial disclosures.

PERSPECTIVE

Roxana Mehran

This is yet another study on a very important topic in decision-making for clinicians who are taking care of patients with STEMI presenting for a primary angioplasty. Many of us have seen patients who have multivessel disease, and the crucial decision of whether you proceed to treat the other vessels at the time of intervention in the same hospital, or in a staged fashion, or not do anything is really an unanswered question.

While we have trials such as CvLPRIT and PRAMI that suggest perhaps we should proceed in treating patients with multivessel disease at the same setting based on those data, this particular trial, interestingly enough, did not show any difference, or benefit, in treating the patients up front. While these are really good trials trying to answer the important questions, none of them are powered to answer the questions in a definitive fashion and therefore are not really changing practice in any way at the moment.

The large randomized COMPLETE study, which is being led by **Shamir Mehta, MD,** at McMaster University, involving over 4,000 patients who present with STEMI and have multivessel disease, in performing complete revascularization vs. staging and waiting will answer a lot of these questions definitively.

However, the PRAGUE 13 study is another body of evidence that actually does not support or refute, does not show harm or show benefit. We still need to wait and see what the large randomized studies will show us.

Roxana Mehran, MD, FACC
Professor of Medicine (Cardiology), Health Evidence and Policy
Director of Interventional Cardiovascular Research and Clinical Trials
Icahn School of Medicine at Mount Sinai
Associate Medical Editor, CARDIOLOGY TODAY'S INTERVENTION

Disclosure: Mehran reports receiving research grants from AstraZeneca, Bristol-Myers Squibb/Sanofi-Aventis, Daiichi Sankyo/Eli Lilly and The Medicines Company and receiving advisory board/consultant fees from Abbott Laboratories, AstraZeneca, Bayer, Boston Scientific, Covidien, CSL Behring, Janssen Pharmaceuticals, Merck, Osprey Medical Inc., Regado Biosciences, Sanofi-Aventis, The Medicines Company and Watermark Consulting.

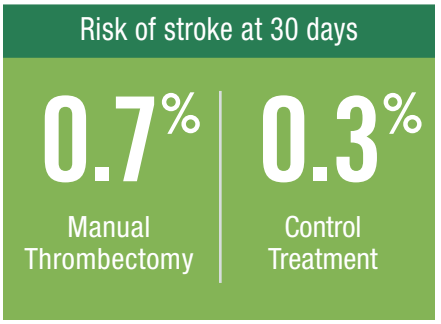
Originally posted on Healio.com/Cardiology | May 29, 2015

TOTAL: Stroke risk associated with manual thrombectomy during PCI evident within 48 hours

The increased stroke risk associated with manual thrombectomy during primary PCI detected in the TOTAL trial was evident within the first 48 hours after the procedure and still prominent at 180 days, according to new data from the TOTAL trial presented at EuroPCR.

The TOTAL trial of 10,732 patients with STEMI undergoing primary PCI, presented at the American College of Cardiology Scientific Sessions in March and published in *The New England Journal of Medicine,* found that patients assigned manual thrombectomy did not achieve a clinical benefit compared with patients assigned control treatment, but had a higher risk for stroke at 30 days (0.7% vs. 0.3%; HR = 2.06; 95% CI, 1.13-3.75).

At EuroPCR, **Sanjit S. Jolly, MD, MSc, FRCPC,** associate professor of medicine and interventional cardiologist at McMaster University, Hamilton, Ontario, presented additional data on stroke from the TOTAL cohort, including stroke timing, severity, subtypes and independent predictors.



The difference between the groups in stroke remained at 180 days (thrombectomy group, 1%; controls, 0.5%; HR = 2; 95% CI, 1.25-3.2), Jolly said.

Much of this difference occurred in those who had a fatal stroke or one resulting in major disability, defined as Rankin score of 3 to 6 (thrombectomy group, 0.7%; controls, 0.3%; HR = 2.69; 95% CI, 1.42-5.08), he said.

At 180 days, compared with controls, the thrombectomy group had a higher rate of both ischemic strokes (0.7% vs. 0.4%; HR = 1.71; 95% CI, 1.03-3) and primary hemorrhagic strokes (0.2% vs. 0.04%; HR = 4.98; 95% CI, 1.09-22.7), according to Jolly.

The time period in which the difference in stroke rate between the groups was statistically significant was 0 to 48 hours after the procedure (thrombectomy group, 0.3%; controls, 0.1%; HR = 3; 95% CI, 1.09-8.25). Patients who had a stroke within 180 days were much more likely to die compared with those who did not have a stroke (30.8% vs. 3.4%; HR = 10.17; 95% CI, 6.7-15.45).

"Routine thrombectomy compared to PCI alone (with only bailout thrombectomy) was associated with an increased risk of stroke that was evident within 48 hours."

SANJIT S. JOLLY, MD, MSC, FRCPC

Independent predictors of stroke included assignment to thrombectomy (HR = 2; 95% CI, 1.24-3.24), age per 10 years (HR = 1.27; 95% CI, 1.04-1.55), female sex (HR = 2.1; 95% CI, 1.31-3.36), peripheral vascular disease (HR = 2.56; 95% CI, 1.09-6.03), previous stroke (HR = 2.54; 95% CI, 1.23-2.54), prior diabetes (HR = 2.41; 95% CI, 1.51-3.85) and use of intra-aortic balloon (HR = 2.98; 95% CI, 1.15-7.73), according to Jolly.

The researchers also performed a meta-analysis and found an increased risk for stroke in the thrombectomy group across 10 trials comparing thrombectomy plus PCI to PCI alone (0.8% vs. 0.5%; OR = 1.59; 95% CI, 1.11-2.27). However, when they performed a meta-analysis of risk for mortality across 20 trials comparing thrombectomy plus PCI to PCI alone, a trend toward a benefit for thrombectomy emerged (3.8% vs. 4.3%; OR = 0.87; 95% CI, 0.76-1).

"Routine thrombectomy compared to PCI alone (with only bailout thrombectomy) was associated with an increased risk of stroke that was evident within 48 hours," Jolly said during a presentation. "Future trials of thrombectomy devices need to carefully collect stroke outcomes … to determine safety in addition to efficacy."

The complete data have since been published online ahead of print in the *European Heart Journal.* – *by Erik Swain*

References:

Jolly SS, et al. Stroke in the TOTAL trial: A randomized trial of routine thrombectomy vs. PCI alone in STEMI. *Eur Heart J.* 2015 June 29 [Epub ahead of print].

Jolly SS, et al. *N Engl J Med.* 2015;doi:10.1056/NEJMoa1415098.

Jolly SS, et al. Hot Line: Primary PCI and STEMI in Practice. Presented at: EuroPCR; May 19-22, 2015; Paris.

Disclosure: The study was funded by Medtronic, the Canadian Network and Centre for Trials Internationally (CANNeCTIN) and the Canadian Institutes of Health Research. Jolly reports receiving grant support from the Canadian Institutes of Health Research, CANNeCTIN and Medtronic, and receiving personal fees from AstraZeneca and St. Jude Medical.

Data on thrombus aspiration from TOTAL trial alter treatment approach in patients with STEMI

The full trial results from the TOTAL trial, published in *The New England Journal of Medicine* and presented at ACC 2015, prompted response from clinicians. **Deepak L. Bhatt, MD, MPH,** chief medical editor of Cardiology Today's Intervention, and **Sahil Parikh, MD,** an interventional cardiologist at the University Hospital Case Medical Center in Cleveland, Ohio, offer in-depth perspectives on this potentially "practice-changing" trial.

Deepak L. Bhatt, MD, MPH

Previously, the thought had been that there might be a reduction in ischemic events with manual aspiration thrombectomy. Meta-analyses of smaller trials done in years past on this topic showed a reduction in all-cause mortality with manual thrombus aspiration and individually a number of the trials showed reductions in stent thrombosis and improvement in a variety of surrogate endpoints. However, TASTE, a large, registry-based, randomized clinical trial, did not find any benefit in the primary endpoint for manual aspiration thrombectomy.


Deepak L. Bhatt

The TOTAL trial was meant to be the tie-breaker to definitely determine whether manual aspiration thrombectomy reduces ischemic events. As it turns out, the trial found no hint of benefit (primary outcome of CV death, recurrent MI, cardiogenic shock or NYHA class IV HF within 180 days: 6.9% vs. 7%; HR = 0.99; 95% CI, 0.85-1.15) and indeed found a significant increase in the rate of stroke (0.7% vs. 0.3%; HR = 2.06; 95% CI, 1.13-3.75) in the patients randomly assigned to manual thrombus aspiration.

Those are not data that would be supportive of routine thrombus aspiration during STEMI, and for that reason I am going to change my practice. This shows that sometimes meta-analyses of small studies can be misleading. Alternatively, maybe times have changed since those studies were done, and now with low-profile, second-generation drug-eluting stents and quicker door-to-balloon times, perhaps the potential benefit of aspiration isn't as great as it used to be.

Also, this trial does not rule out the possibility that patients with large thrombus burden may still benefit from manual aspiration thrombectomy. So I wouldn't go so far as to say it should never be done, but certainly on the basis of this trial and TASTE, it should not be part of routine primary PCI.

Sahil Parikh, MD

The TOTAL trial, which looked at over 2,500 patients, with a randomization to mandated aspiration thrombectomy vs. bailout thrombectomy in the setting of STEMI PCI, was very impactful. It was interesting that there was no benefit with respect to CV morbidity or mortality, with respect to using either pre-thrombectomy in all cases vs. as a bailout, and there was a signal now for harm, which was in contra-distinction from earlier trials, where there was no demonstrated benefit but there wasn't necessarily a harm.


Sahil Parikh

It kind of puts to rest the concern that many had about whether thrombectomy was a necessary part of your index PCI with primary STEMI revascularization. On an everyday basis, in my practice, it will make a difference in how I approach patients. ■

Trial Scorecard

INTERVENTION

TOTAL
The Trial of Routine Aspiration Thrombectomy with PCI vs. PCI Alone in Patients with STEMI

Researchers assessed the composite of death from CV causes, recurrent MI, cardiogenic shock or HF within 180 days as primary outcome, with a key safety outcome of stroke within 30 days, among patients with STEMI undergoing primary PCI with routine upfront manual aspiration thrombectomy vs. PCI alone.

Design:	prospective, randomized
Patients:	10,732
Centers:	multicenter
Countries:	international

RESULTS: The primary outcome occurred in 347 of 5,033 patients (6.9%) with thrombectomy vs. 351 of 5,030 patients (7%) with PCI alone (HR with thrombectomy = 0.99; 95% CI, 0.85-1.15). Rates of CV death (3.1% with thrombectomy vs. 3.5% with PCI alone; HR = 0.9; 95% CI, 0.73-1.12) and primary outcome plus stent thrombosis or target-vessel revascularization (9.9% vs. 9.8%; HR = 1; 95% CI, 0.89-1.14) were similar. Stroke occurred in 33 patients (0.7%) with thrombectomy vs. 16 patients (0.3%) with PCI alone (HR = 2.06; 95% CI, 1.13-3.75).

Jolly SS, et al. N Engl J Med. *2015;doi:10.1056/NEJMoa1415098.*

Cardiology today

Read more executive summaries of the latest important cardiology trials at **Healio.com/Cardio/TrialScorecards**

Originally posted on Healio.com/Cardiology | April 23, 2015

Shorter hospital stay safe for older patients undergoing PCI for STEMI

Patients aged at least 65 years discharged from the hospital as early as 48 hours after primary PCI for STEMI had similar outcomes compared with patients who stayed in the hospital for 4 to 5 days.

Rajesh V. Swaminathan

Researchers studied the safety of a shorter hospital stay in 33,920 patients with STEMI in the linked CathPCI Registry-CMS dataset. Eligible participants were aged at least 65 years and underwent primary PCI from 2004 to 2009.

Thirty-day outcomes were analyzed for three groups based on length of hospital stay: up to 3 days (26.9%); 4 to 5 days (46.3%); and at least 5 days (26.8%).

Longer length of stay was more common in older patients, women and those with comorbidities such as cardiogenic shock and multivessel disease. Higher ejection fraction and single-vessel disease were more common in patients with a shorter length of stay.

The researchers reported no significant difference in the rate of 30-day all-cause mortality between a length of stay of 4 to 5 days compared with up to 3 days (HR = 1; 95% CI, 0.74-1.34). Similarly, rates of MACE, defined as death, readmission for MI or unplanned revascularization, were not different for a length of stay of 4 to 5 days compared with up to 3 days (HR = 1.03; 95% CI, 0.86-1.25).

However, rates of adjusted mortality (HR = 2.3; 95% CI, 1.72-3.07) and MACE (HR = 1.75; 95% CI, 1.44-2.12) were significantly increased with a length of stay of at least 5 days compared with up to 3 days.

The researchers also evaluated outcomes associated with very short length of stay of 1 to 2 days, with discharge on the day of or day after primary PCI. A very short length of stay was associated with significantly worse outcomes at 30 days. Compared with very short length of stay, patients who stayed in the hospital for 3 to 4 days had a more than 50% reduction in adjusted mortality and a more than 40% reduction in MACE.

"These data suggest that early discharge (but not within 48 [hours] after [primary] PCI) may be safe among selected older patients undergoing [primary] PCI for STEMI who do not develop in-hospital complications," the researchers concluded. – *by Rob Volansky*

Reference:
Swaminathan RV, et al. *J Am Coll Cardiol.* 2015;doi:10.1016/j.jacc.2015.01.028.

Disclosure: Swaminathan reports no relevant financial disclosures.

Originally posted on Healio.com/Cardiology | March 20, 2015

No evidence of 'smoker's paradox' found in STEMI registry

Previous research has suggested that patients with ACS who smoke have lower mortality than nonsmokers, but results from a large, single-center registry of patients with STEMI who underwent PCI indicate no evidence of a smoker's paradox.

Researchers in the United Kingdom studied differences between smokers and nonsmokers in a registry including all patients admitted with acute STEMI undergoing primary PCI in South Yorkshire, England, from January 2009 to June 2012.

Lloyd Steele, MBChB, of the Imperial College NHS Trust, told Cardiology Today that no large single-center registry had previously been undertaken to evaluate the smoker's paradox in patients with STEMI patients in the PCI era.

The analysis included 1,715 STEMI events in 1,680 patients. Of those, 49.1% of patients were smokers, 27.2% former smokers and 23.7% nonsmokers. One hundred fourteen patients (6.6%) died after 1 year. Researchers reported data on the smoking status of 99 deceased patients (87%) and 1,562 surviving patients (98%).

Smoking was associated with better survival at 1 year after STEMI compared with nonsmokers and former smokers ($P = .4$).

Age was identified as a significant confounder ($P = .001$). The average age upon presentation of STEMI was 57 years for smokers compared with 66 years for nonsmokers and 68 years for former smokers.

"When we adjusted for age and gender, we found that smokers seemed to have a worse outcome," Steele said. After adjustment, the rate of 1-year survival was worse among current smokers (HR = 1.3; 95% CI, 0.77-2.2) compared with former smokers (HR = 1.03; 95% CI, 0.61-1.75) and nonsmokers (HR = 1); however, this difference was not significant ($P = .55$).

"In this large, single-center registry of STEMI patients managed by primary PCI, we did not find any evidence of the 'smoker's paradox,'" the researchers concluded. – *by Rob Volansky*

Reference:
Steele L, et al. Poster 1107-115. Presented at: American College of Cardiology Scientific Sessions; March 14-16, 2015; San Diego.

Disclosure: The researchers report no relevant financial disclosures.

Originally posted on Healio.com/Cardiology | March 26, 2015

Complete revascularization benefits patients with multivessel CAD requiring PCI

Among patients with STEMI and multivessel CAD undergoing primary PCI, those who had complete revascularization had better outcomes than those who had revascularization of the culprit vessel only, according to results of the DANAMI3-PRIMULTI study.

Thomas Engstrøm

Thomas Engstrøm, MD, DMSci, PhD, and colleagues randomly assigned 627 patients with STEMI and multivessel CAD, defined as more than 50% stenosis in at least one nonculprit lesion of at least 2 mm, to undergo PCI of the culprit lesion only or complete revascularization guided by fractional flow reserve.

Approximately 30% to 50% of patients admitted for STEMI have stenoses in vessels other than the infarct-related artery, Engstrøm said during a press conference at the American College of Cardiology Scientific Sessions. "Guidelines have previously supported that you [revascularize] only the culprit vessel and leave the other vessels untreated, but two very recent studies suggest a benefit for revascularization of all the coronary arteries," said Engstrøm, chief consultant, department of invasive cardiology, Rigshospitalet, University of Copenhagen, Denmark.

Patients admitted for STEMI

30%–50% Have stenoses in **VESSELS OTHER THAN** the infarct-related artery

The primary endpoint of the DANAMI3-PRIMULTI study was a composite of all-cause mortality, nonfatal MI and ischemia-driven revascularization of nonculprit lesions. All patients were followed for at least 1 year.

Compared with PCI of the culprit lesion only, patients assigned complete revascularization had a lower risk for the primary endpoint (HR = 0.56; 95% CI, 0.38-0.83).

The results were driven by ischemia-driven revascularization of nonculprit lesions (HR = 0.31; 95% CI, 0.18-0.53), Engstrøm said.

There was no difference between the groups in nonfatal MI (HR = 0.94; 95% CI, 0.47-1.9) or all-cause death (HR = 1.4; 95% CI, 0.63-3).

"Complete FFR-guided revascularization of multivessel disease in STEMI patients reduces the primary endpoint of all-cause death, reinfarction and complete revascularization, but we acknowledge also that this endpoint was not driven by hard endpoints," he said. "Having said that, it turned out that 40% of the repeat revascularizations were urgent on the basis of unstable angina." – *by Erik Swain*

PERSPECTIVE

Sripal Bangalore

Despite complete revascularization being a class III indication (do not do), the issue of what to do for significant nonculprit artery blockages has been increasingly studied.

Two recent studies showed significant benefit of complete revascularization when compared with culprit-only revascularization. This is yet another trial which shows similar results — advantage of complete revascularization over culprit-only — thus questioning the validity of the guideline recommendations.

That being said, all three trials showed significant benefit for the reduction in repeat procedures but no difference in harder outcomes of death or MI.

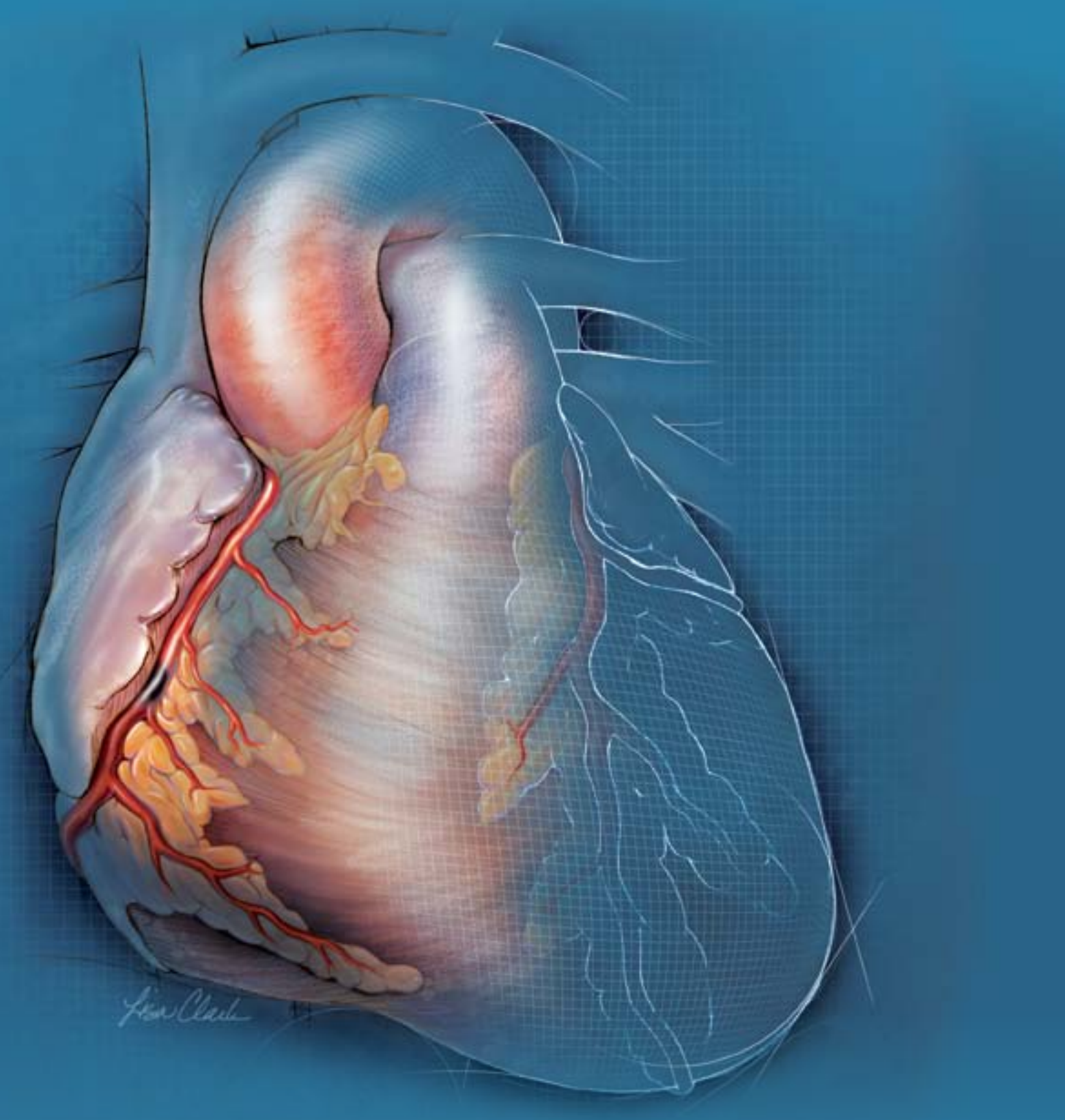
We need larger studies to answer the question of whether complete revascularization will indeed reduce the risk for death or MI. Nevertheless, it is time the guidelines are updated to allow for complete revascularization.

Sripal Bangalore MD, MHA, FACC, FAHA, FSCAI
Director of Research, Cardiac Catheterization Laboratory
Director, Cardiovascular Outcomes Group
Associate Professor of Medicine
New York University School of Medicine

Disclosure: Bangalore reports no relevant financial disclosures.

Reference:
Engstrøm T. Late-Breaking Clinical Trials V: TCT@ACC-i2 Interventional Cardiology. Presented at: American College of Cardiology Scientific Sessions; March 14-16, 2015; San Diego.

Disclosure: Engstrøm reports receiving consulting fees/honoraria from Eli Lilly, New Zealand Pharma, Novo Nordisk and Servier.



SLACK
INCORPORATED

Delivering the best in health care information and education worldwide

6900 Grove Road, Thorofare, NJ 08086 USA
phone: 856-848-1000 • www.Healio.com