High On-Treatment Platelet Reactivity as a Risk Factor for Secondary Prevention After Coronary Stent Revascularization
A Landmark Analysis of the ARCTIC Study

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Background—Individualizing antiplatelet therapy after platelet function testing did not improve outcome after coronary stenting in the Assessment by a Double Randomization of a Conventional Antiplatelet Strategy Versus a Monitoring-Guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption Versus Continuation One Year After Stenting (ARCTIC) study. Whether results are different during the phase of secondary prevention starting after hospital discharge, when periprocedural events have been excluded, is unknown.

Methods and Results—In ARCTIC, 2440 patients were randomized before coronary stenting to a strategy of platelet function monitoring (VerifyNow P2Y₁₂/aspirin point-of-care assay) with drug adjustment in suboptimal responders to antiplatelet therapy or to a conventional strategy without monitoring and without drug or dose changes. We performed a landmark analysis starting at the time of hospital discharge evaluating the primary end point of death, myocardial infarction, stent thrombosis, stroke, or urgent revascularization through 1 year. After discharge, the primary end point occurred in 8.6% of patients in the monitoring arm and 7.9% in the conventional arm (hazard ratio, 1.105; 95% confidence interval, 0.835–1.461; \( P = 0.48 \)). Stent thrombosis or urgent revascularization occurred in 4.4% and 4.5% in the monitoring and conventional arms, respectively (\( P = 0.99 \)). There was no difference for any of the other ischemic end points. Major bleeding event rates were 1.8% in the monitoring arm and 2.8% in the conventional arm (\( P = 0.11 \)), whereas major or minor bleeding event rates were 2.3% and 3.4%, respectively (\( P = 0.10 \)).

Conclusions—Detection of platelet hyper-reactivity by platelet function testing in patients undergoing coronary stenting with further therapeutic adjustment does not reduce ischemic recurrences after intervention. On-treatment platelet hyperreactivity cannot be considered as a risk factor requiring intervention for secondary prevention after percutaneous coronary revascularization.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00827411.

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Key Words: percutaneous coronary intervention ■ platelet aggregation inhibitors ■ platelet function tests
Although high on-treatment platelet reactivity in coronary patients is a marker of ischemic risk and biological information potentially available to adjust antiplatelet therapy, few randomized studies have been unable to establish differences in clinical outcomes with platelet function monitoring and treatment adjustment for coronary stenting compared with standard antiplatelet therapy without monitoring.1–3 The Assessment by a Double Randomization of a Conventional Antiplatelet Strategy Versus a Monitoring-Guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption Versus Continuation One Year After Stenting (ARCTIC) study was unique in the fact that poor response to both aspirin and clopidogrel was searched for and treated, starting before intervention to prevent periprocedural and long-term events.3 No hint of improvement in ischemic outcomes was observed from randomization performed before the interventional procedure to the 1-year follow-up. Because randomization occurred early, most events were periprocedural myocardial infarctions. We wondered whether results would differ when considering patients only after hospital discharge when patients are on maintenance therapy to prevent new clinical ischemic events once they have returned home.

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Whether individualized treatment of platelet hyperreactivity, considered as a new risk factor, can improve secondary prevention during the first year after hospital discharge after coronary stenting is unknown. The ARCTIC trial provides an opportunity to examine this question. We performed a landmark analysis starting at the time of hospital discharge, evaluating the primary composite end point of death, myocardial infarction, stent thrombosis, stroke, or urgent revascularization over 1 year, as well as all the other prespecified secondary end points.

Methods

Study Design and Population

ARCTIC was a randomized study recruiting patients scheduled for planned drug-eluting stent implantation at 38 centers in France. Primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction, planned use of glycoprotein IIb/IIIa inhibitors, long-term anticoagulation therapy, and bleeding diathesis were exclusion criteria. The study protocol was registered at www.ClinicalTrials.gov under the number NCT00827411, and the main results have been published previously.1 Written informed consent was obtained from all patients. Eligible patients were centrally randomized to a strategy of platelet function evaluation with adjustment of antiplatelet drugs and doses in patients with inadequate platelet inhibitory response (monitoring arm) or to a conventional strategy of treatment without platelet function assessment (conventional arm). In the monitoring arm, platelet function measurements were performed for both aspirin and P2Y12 inhibitors. The same measurements were repeated 2 to 4 weeks after discharge for further adjustment of maintenance therapy in case of persistent inadequate response to treatment. The treatment adjustments in the monitoring arm could be performed both ways, and antiplatelet therapy could be reduced in case of hyporesponsiveness to treatment. Platelet function monitoring was performed with the VerifyNow assay (Accumetrics, San Diego, CA), a point-of-care platelet function test that uses 2 different cartridges for aspirin and clopidogrel. An algorithm for drug and dose adjustments in the monitoring group was provided to all investigators. The 14- to 30-day time point measurement allowed adjustment of the maintenance dose (MD) of thienopyridine or aspirin. Patients with high on-thienopyridine platelet reactivity were switched either to prasugrel 10-mg MD or to a 75-mg increase in clopidogrel MD. Patients without high on-thienopyridine platelet reactivity remained on the same thienopyridine MD, and those with very low on-thienopyridine MD, and those with very low on-thienopyridine platelet reactivity, defined as a percent inhibition >90%, were switched to clopidogrel 75-mg MD if on prasugrel 10-mg or clopidogrel 150-mg MD.2 Patients with optimal platelet reactivity after testing were left with the same treatment for the rest of the study.

The primary end point was the composite of all-cause death, myocardial infarction, stroke or transient ischemic attack, urgent coronary revascularization, and stent thrombosis. All definitions have been described elsewhere.1,3,4 The main secondary efficacy end point was the composite of stent thrombosis (rescued or not) and urgent revascularization. All the other prespecified end points of the study protocol were also analyzed. The main safety end point was defined as major bleeding using the percutaneous coronary intervention–specific Safety and Efficacy of Enoxaparin in Percutaneous Coronary Intervention Patients, an International Randomized Evaluation (STEEPLE) definitions.5 All events were adjudicated by an independent Clinical Events Committee, the members of which were unaware of treatment assignments.

Statistical Analysis

The analysis was based on all events that occurred in the intention-to-treat population, defined as all randomized patients who
signed an informed consent form. In case of patients withdrawing consent during the study, only their data collected before the day of withdrawal were included in the database. The end points were analyzed with the use of a Cox model. We performed an additional analysis adjusting for clinically relevant baseline characteristics (age, sex, weight, diabetes mellitus, smoking, prior myocardial infarction) that were included in the Cox regression model. When performing the landmark analyses from discharge to the end of the trial, we ascertained that the number of patients at risk included all patients who were alive with any available information after discharge, regardless of whether a nonfatal event had occurred during the hospital stay. All patients were censored at the date of last available information. The 95% confidence interval of the hazard ratio is presented. For baseline characteristics of patients in the landmark analysis for 1-year discharge, normality of quantitative variables was tested by the Shapiro-Wilk test. Because in our study they were found to be non-Gaussian, they were summarized as median (quartiles) and compared by use of Mann-Whitney test. The χ² test for frequency comparisons was used. All tests were made at a 2-sided 5% significance level with SAS version 9.2 (SAS Institute Inc.).

The trial and the statistical analyses were performed by the non-profit academic research organization ACTION (Allies in Cardiovascular Trials, Initiatives and Organized Networks), based at Pitié-Salpêtrière Hospital (www.action-coeur.org). Research grants were obtained from Fondation de France, Sanofi-Aventis, Cordis, Medtronic, Boston Scientific, and Fondation SGAM, which had no involvement in the conduct of the study.

### Results

#### Patients and Treatments

A total of 2440 patients were enrolled, of whom 1227 were assigned to the conventional group and 1213 to the monitoring group. Of those, 1191 patients in the conventional group and 1194 patients in the monitoring group were evaluated in the landmark analysis starting at hospital discharge (Figure 1). Baseline characteristics of the population were well matched in the 2 study groups, including for the main landmark analysis of the present study related to outcomes after hospital discharge (Table 1). In the monitoring arm, high on-aspirin platelet reactivity and high on-clopidogrel platelet reactivity were detected before stent implantation in 7.6% and 34.5% of patients, respectively, and led to treatment adjustments in the catheterization laboratory. When on-treatment platelet reactivity measurements were repeated 2 to 4 weeks after hospital discharge, high on-aspirin platelet reactivity was found in 3.9% of patients and high on-clopidogrel platelet reactivity in 15.6% of patients. Treatments were further adjusted according to the prespecified algorithms and were not controlled again during the year of treatment. After monitoring 2 to 4 weeks after discharge, 11.2% of patients had their thienopyridine treatment decreased (prasugrel toward clopidogrel or lower dose of clopidogrel) because of low on-thienopyridine platelet reactivity, and 10.8% of patients had their clopidogrel dose increased or changed toward prasugrel because of high on-thienopyridine platelet reactivity on a treatment that was thought not to be maximal yet. On the basis of the aspirin reaction unit values obtained at day 14, the aspirin dose was decreased in 3.4% of patients and increased in 3.1% of patients. Antiplatelet therapy in the control arm was left to the discretion of the investigators and decided on without platelet function testing being performed.

#### Efficacy End Points

The event rates from randomization to hospital discharge did not differ significantly between the 2 groups (Table 2). A nonsignificant trend was observed for more frequent in-hospital death or resuscitated cardiac arrest during the hospital period in the monitoring arm (P=0.06). The number of events for the primary end point between hospital discharge and 1-year follow-up represents 22.9% of all the events accumulated over the period from randomization to the 1-year follow-up. After discharge, the primary end point occurred in 103 of 1194 patients in the monitoring arm and 94 of 1191 in the conventional arm (P=0.48; Table 3 and Figure 2). Consistent results were found for the main secondary end point and across all secondary end points (Table 3 and Figure 3). All the results were also confirmed when the Cox regression model was adjusted for important clinical variables in the analyses performed both before and after the landmark cut point.

The primary end point rate in the 1-year follow-up period increased modestly and not significantly across tertiles of high platelet reactivity measured 2 to 4 weeks after discharge. The
rates were 7.6%, 8.3%, and 9.7% across the 3 tertiles of P2Y₁₂ reaction units \( (P=NS) \) and 6.4%, 8.5%, and 10.5% across the 3 tertiles of aspirin reaction units \( (P=NS) \).

**Safety End Points**

Major bleeding did not differ between the 2 groups during the hospital stay or during the 1-year period after hospital discharge (Tables 2 and 3). STEEPLE major bleeding occurred in 33 of 1191 patients in the control arm and 21 of 1194 in the monitoring arm after hospital discharge \( (P=0.11) \). STEEPLE major or minor bleeding also tended to be less frequent in the monitoring group after hospital discharge \( (P=0.10) \). These results were confirmed when the Cox regression model was adjusted for important clinical variables in the analyses performed both before and after the landmark cut point.

The rates of major or minor bleeding in the 1-year follow-up period increased numerically across tertiles of high platelet reactivity measured 2 to 4 weeks after discharge. The rates were 1.5%, 2.0%, and 3.3% across the 3 tertiles of P2Y₁₂ reaction units \( (P=NS) \) and 1.3%, 2.0%, and 3.6% across the 3 tertiles of aspirin reaction units \( (P=NS) \).

**Discussion**

It has been suggested that high on-treatment platelet reactivity is a risk factor for ischemic events in coronary artery disease, particularly after coronary stenting. \(^6–10\) Measurement of this biological risk factor with point-of-care assays has led to the possibility of treating this risk factor as we are used to with glycemia or low-density lipoprotein cholesterol for secondary prevention. In the present study, high on-treatment platelet reactivity was identified in patients allocated by randomization to the strategy of platelet function monitoring, and treatments were adjusted to control this risk factor as much as possible both before and after hospital discharge. However, this strategy failed to show a benefit on ischemic events that occur during the first year after hospitalization for revascularization with coronary stenting. The present analysis focused on the secondary prevention phase by excluding all in-hospital events and confirms the global results of the study. High on-treatment platelet reactivity is not only a marker of risk but also a risk factor that we can possibly modify with the antiplatelet drugs available. However, our findings suggest that the modifications of treatment do not affect clinical outcome. This has been observed before with other biomarkers such as high-density lipoprotein cholesterol or triglycerides, which are also modifiable risk factors, with, however, no demonstration of a clinical benefit of an intervention on the level of these risk factors. \(^11,12\) The risk-to-benefit ratio of interventions designed to modify risk factors can vary, depending on multiple beneficial or harmful effects beyond their effect on the risk factor. Some strategies are known to improve patient outcomes, whereas others affect only risk factor levels. Our data add to the evidence that a strategy aiming only at controlling platelet reactivity, considered as a risk factor, may not predict
its effect on patient outcomes. However, these findings do not call into question the benefit of dual antiplatelet therapy after coronary stenting, for which there is paramount evidence. The present analysis adds considerably to the understanding of the value of a platelet function–guided strategy to improve the clinical response to antiplatelet therapy after coronary revascularization with a drug-eluting stent. The landmark analyses reported here provide an additional step in understanding the disconnect between the achievement of an optimal on-treatment platelet reactivity and the improvement in clinical

### Table 3. Ischemic and Bleeding End Points From Hospital Discharge to End of Follow-Up (Percentages Are Kaplan-Meier Estimates)

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Conventional Treatment (n=1191), %</th>
<th>Monitoring Treatment (n=1194), %</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any death, myocardial infarction, stent thrombosis, stroke or TIA, urgent revascularization (primary end point)</td>
<td>8.2</td>
<td>9.1</td>
<td>1.105 (0.835–1.461)</td>
<td>0.4848</td>
</tr>
<tr>
<td>Stent thrombosis (revascularized or not) or any urgent revascularization (main secondary)</td>
<td>4.7</td>
<td>4.7</td>
<td>1.002 (0.685–1.467)</td>
<td>0.9906</td>
</tr>
<tr>
<td>Any death, recurrent ACS, stroke or TIA</td>
<td>6.8</td>
<td>7.2</td>
<td>1.057 (0.773–1.443)</td>
<td>0.7296</td>
</tr>
<tr>
<td>Death or resuscitated cardiac arrest</td>
<td>1.7</td>
<td>2.1</td>
<td>1.220 (0.665–2.241)</td>
<td>0.5204</td>
</tr>
<tr>
<td>Death or myocardial infarction</td>
<td>4.8</td>
<td>5.4</td>
<td>1.117 (0.776–1.608)</td>
<td>0.5530</td>
</tr>
<tr>
<td>Any death, myocardial infarction, stent thrombosis revascularized or not, stroke or TIA, urgent revascularization, STEEPLE major bleed (net clinical benefit)</td>
<td>9.8</td>
<td>10.2</td>
<td>1.043 (0.804–1.352)</td>
<td>0.7523</td>
</tr>
<tr>
<td>Any death</td>
<td>1.7</td>
<td>2.1</td>
<td>1.167 (0.632–2.156)</td>
<td>0.6225</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3.6</td>
<td>4.0</td>
<td>1.105 (0.723–1.686)</td>
<td>0.6452</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0.5</td>
<td>0.9</td>
<td>1.678 (0.610–4.617)</td>
<td>0.3162</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>0.4</td>
<td>0.5</td>
<td>1.211 (0.370–3.968)</td>
<td>0.7519</td>
</tr>
<tr>
<td>Urgent revascularization</td>
<td>4.4</td>
<td>4.5</td>
<td>1.002 (0.677–1.483)</td>
<td>0.9926</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STEEPLE major bleeding</td>
<td>2.9</td>
<td>1.9</td>
<td>0.638 (0.369–1.103)</td>
<td>0.1078</td>
</tr>
<tr>
<td>STEEPLE minor bleeding</td>
<td>1.0</td>
<td>0.7</td>
<td>0.731 (0.294–1.818)</td>
<td>0.5009</td>
</tr>
<tr>
<td>STEEPLE major or minor bleeding</td>
<td>3.6</td>
<td>2.4</td>
<td>0.661 (0.407–1.075)</td>
<td>0.0954</td>
</tr>
<tr>
<td>TIMI major bleeding</td>
<td>0.6</td>
<td>0.3</td>
<td>0.575 (0.168–1.966)</td>
<td>0.3780</td>
</tr>
<tr>
<td>TIMI minor bleeding</td>
<td>1.1</td>
<td>0.7</td>
<td>0.621 (0.257–1.498)</td>
<td>0.2892</td>
</tr>
<tr>
<td>TIMI major or minor bleeding</td>
<td>1.8</td>
<td>1.1</td>
<td>0.605 (0.296–1.237)</td>
<td>0.1687</td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; CI, confidence interval; HR, hazard ratio; STEEPLE, Safety and Efficacy of Enoxaparin in Percutaneous Coronary Intervention Patients, an International Randomized Evaluation; TIA, transient ischemic attack; and TIMI, Thrombolysis in Myocardial Infarction.

**Figure 2.** Kaplan-Meier curve of proportion of patients with primary outcome events (any death, myocardial infarction, stent thrombosis, stroke or transient ischemic attack, and urgent revascularization) after discharge up to 1-year follow-up. HR indicates hazard ratio.
outcome. In ARCTIC, like in the Gauging Responsiveness With a VerifyNow Assay–Impact on Thrombosis and Safety (GRAVITAS), Clopidogrel Optimal Loading Dose Usage to Reduce Recurrent Events (CURRENT), Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY), and A Comparison of Prasugrel at PCI or Time of Diagnosis of Non-ST Elevation Myocardial Infarction (ACCOAST) trials, lower platelet reactivity obtained with stronger P2Y12 inhibition was not associated with improved ischemic outcomes.1,13–16 The benefit of this class of drugs appears to depend not only on the drug and dose effects but also on the clinical situation, which includes recent stenting, the risk level of the population, and the time and appropriateness of drug administration.

We believe that the design of our study is optimal to answer the question of detection of this new risk factor (on-treatment platelet reactivity) with intensification of platelet inhibition in patients with a poor response to clopidogrel or aspirin to improve clinical outcome. Although a few other studies had different designs, all the conclusions are consistent across the randomized studies. All these studies dealt more or less with stable patients undergoing coronary stenting. We cannot exclude a benefit of platelet function testing to adjust therapy in higher-risk patients. The ongoing Treatment With Adenosine Diphosphate (ADP) Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome (TRANSLATE-POPS; NCT01088503) study and Tailored Antiplatelet Therapy Versus Recommended Dose of Prasugrel (ANTARCTIC; NCT01538446) study will address the question of platelet function testing to guide antiplatelet therapy in higher-risk populations.17 Our conclusions may not apply directly to other platelet function tests or the same test using different cutoff values to trigger treatment adjustments, although it is unlikely that the conclusions would differ much.18 Along the same line, our conclusions cannot be extended to genetic profiling, and recent studies suggest that genetic testing may effectively guide the choice of antiplatelet therapy in patients at low or high risk (Identification of Clopidogrel CYP2C19 Metabolizer and Thienopyridine Treatment After an Acute Coronary Syndrome; NCT01390974).19–21 However, a clinical trial comparable to ARCTIC still needs to be performed with genetic testing.

Our study has a number of limitations, including the fact that this analysis was not prespecified but was required at some point to sort out the acute from the chronic effects of the strategy of monitoring with treatment adjustment. It should also be noted that a limitation of landmark analysis is that the original effects of randomization at entry into the trial are no longer present because of deaths or dropouts before the time of the landmark cut point. To alleviate this issue of landmark analysis, we presented the baseline characteristics of the patients that were well balanced between the 2 groups at the time of the landmark cut point. Moreover, we adjusted for important characteristics that were included in the Cox regression model, and we confirmed the unadjusted results. There is a precedent for landmark analyses in cardiology,22,23 but because of the observational nature of landmark methodology, the findings should be interpreted in the context of cumulative survival analyses from randomization to the end of the study. The cut point of the landmark analysis was taken arbitrarily because it corresponds well to the period of maintenance therapy and secondary prevention. We performed sensitivity analyses (data not shown) with a different cut point (day 30), which confirmed the results presented here. Finally, this study, like previous studies, may lack power to draw definite conclusions, but the consistency of the results across the randomized studies suggests that our conclusions are valid.2,3,8

Conclusions
Our data do not suggest searching for high on-treatment platelet reactivity in patients undergoing stent revascularization to further adjust antiplatelet treatment because this strategy did not reduce ischemic recurrences in the first year after the intervention. Subsequently, high on-treatment platelet reactivity cannot be considered as a risk factor requiring incremental...
antiplatelet treatment for secondary prevention after percutaneous coronary revascularization.

Disclosures

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References

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Whether individualized treatment of platelet hyperreactivity, considered as a new risk factor after coronary stenting, can improve secondary prevention during the first year after hospital discharge is unknown. The landmark analysis of the Assessment by a Double Randomization of a Conventional Antiplatelet Strategy Versus a Monitoring-Guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption Versus Continuation One Year After Stenting (ARCTIC) trial, starting at the time of hospital discharge with platelet function testing for aspirin and thienopyridine, evaluated this hypothesis of antiplatelet treatment adjustment. The results suggest that there is no benefit of such an individualized treatment strategy. Subsequently, high on-treatment platelet reactivity cannot be considered as a risk factor requiring incremental antiplatelet treatment for secondary prevention after percutaneous coronary revascularization with drug-eluting stent implantation.
High On-Treatment Platelet Reactivity as a Risk Factor for Secondary Prevention After Coronary Stent Revascularization: A Landmark Analysis of the ARCTIC Study


for the ARCTIC Investigators

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