Long-term Efficacy of Bivalirudin and Provisional Glycoprotein IIb/IIIa Blockade vs Heparin and Planned Glycoprotein IIb/IIIa Blockade During Percutaneous Coronary Revascularization
REPLACE-2 Randomized Trial

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Context In the Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE)-2 trial, bivalirudin with provisional glycoprotein IIb/IIIa (Gp IIb/IIIa) inhibition was found to be noninferior to heparin plus planned Gp IIb/IIIa blockade in the prevention of acute ischemic end points and was associated with significantly less bleeding by 30 days after percutaneous coronary intervention (PCI).

Objective To determine whether the efficacy of bivalirudin remains comparable with that of heparin plus Gp IIb/IIIa blockade over 6 months and 1 year.

Design, Setting, and Participants Follow-up study to 1 year of a randomized, double-blind trial conducted among 6010 patients undergoing urgent or elective PCI at 233 community or referral hospitals in 9 countries from October 2001 through August 2002.

Interventions Patients were randomly assigned to receive intravenously bivalirudin (0.75 mg/kg bolus, 1.75 mg/kg per hour for the duration of PCI), with provisional Gp IIb/IIIa inhibition, or to receive heparin (65 U/kg bolus), with planned Gp IIb/IIIa inhibition (abciximab or eptifibatide). Both groups received daily aspirin and a thienopyridine for at least 30 days after PCI.

Main Outcome Measures Incidence of death, myocardial infarction, or repeat revascularization by 6 months and death by 12 months after enrollment.

Results At 6 months, death occurred in 1.4% of patients in the heparin plus Gp IIb/IIIa group and in 1.0% of patients in the bivalirudin group (hazard ratio [HR], 0.70; 95% confidence interval [CI], 0.43-1.14; P = .15). Myocardial infarction occurred in 7.4% and 8.2% of patients, respectively (HR, 1.12; 95% CI, 0.93-1.34; P = .24), and repeat revascularization was required in 11.4% and 12.1% of patients, respectively (HR, 1.06; 95% CI, 0.91-1.23; P = .45). By 1 year, death occurred in 2.46% of patients treated with heparin plus Gp IIb/IIIa blockade and in 1.89% of patients treated with bivalirudin (HR, 0.78; 95% CI, 0.55-1.11; P = .16). Nonsignificant trends toward lower 1-year mortality with bivalirudin were present in all patient subgroups analyzed and were of greatest magnitude among high-risk patients.

Conclusion Long-term clinical outcome with bivalirudin and provisional Gp IIb/IIIa blockade is comparable with that of heparin plus planned Gp IIb/IIIa inhibition during contemporary PCI.

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terest therefore remains in the development of newer antithrombotic agents that may further improve outcomes during PCI.

The direct thrombin inhibitor bivalirudin is under investigation as a replacement for heparin in a broad spectrum of patients with ischemic vascular disease.5-9 The Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE)-2 trial recently demonstrated that intraprocedural administration of bivalirudin, with provisional Gp IIb/IIIa blockade (required in 7.2% of patients), provides similar protection from acute ischemic events with significantly fewer hemorrhagic complications as a regimen of heparin plus planned Gp IIb/IIIa inhibition during elective or urgent PCI.10 Among the more than 6000 patients randomized in that trial, the composite ischemic end point of death, myocardial infarction, or urgent repeat revascularization by 30 days occurred in 7.6% and 7.1% of those treated with bivalirudin vs heparin plus Gp IIb/IIIa, respectively, meeting formal statistical criteria for noninferiority. Major in-hospital bleeding rates were significantly reduced with bivalirudin from 4.1% to 2.4% (P<.001).

To assess the durability of the early treatment effect of bivalirudin relative to heparin plus Gp IIb/IIIa, we herein report the results of prospective follow-up of ischemic events through 6 months and survival through 1 year among patients in the REPLACE-2 trial.

METHODS

Patients

The design, methods, and primary results of REPLACE-2 have been previously reported.10 Briefly, 6010 patients undergoing urgent or elective PCI with an approved device at 233 community or referral hospitals in 9 countries in North America, Europe, and Israel were enrolled between October 2001 through August 2002 in this randomized, double-blind, active-controlled trial. Patients undergoing immediate catheter-based reperfusion for acute myocardial infarction were excluded from entry, as were those who required ongoing warfarin therapy or had been treated with unfractionated heparin within the 6 hours (unless activated partial thromboplastin time was ≤50 seconds or activated clotting time was ≤175 seconds), low-molecular-weight heparin within the 8 hours, bivalirudin within the 24 hours, abciximab within the 7 days, or eptifibatide or tirofiban within the 12 hours prior to randomization. Other exclusion criteria included age younger than 18 years, poorly controlled hypertension (blood pressure >180/110 mm Hg), unprotected left main trunk stenosis of more than 50% severity, pregnancy, PCI within the prior 1 month or planned staged PCI within the subsequent month, active internal bleeding or bleeding diathesis, surgery, trauma or gastrointestinal or genitourinary tract bleeding within the prior 6 weeks, prior intracranial bleeding or structural abnormality, platelet count less than 100,000/µL, or renal insufficiency with serum creatinine more than 4 mg/dL (≥335.6 µmol/L) or dependency on renal dialysis. The protocol was approved by the institutional review board at each clinical site, and all patients gave written informed consent.

Study Protocol

Patients were randomly assigned in a double-blind fashion by a central telephone system in a 1:1 ratio to receive intravenously either bivalirudin (0.75 mg/kg bolus prior to the start of PCI, followed by infusion of 1.75 mg/kg per hour for the procedure duration) with provisional Gp IIb/IIIa blockade (if necessary during the procedure) or intravenous heparin bolus of 65 U/kg (maximum 7000 U) with planned Gp IIb/IIIa inhibition. The interventional operator was required to specify the choice of abciximab (0.25-mg/kg bolus, and 0.125 µg/kg per minute [maximum of 10 µg/min] by infusion for 12 hours) or eptifibatide (two 180-µg/kg boluses 10 minutes apart and 2.0 µg/kg per minute by infusion for 18 hours) as the Gp IIb/IIIa inhibitor prior to randomization. Suggested indications for use of provisional Gp IIb/IIIa inhibitor (in the bivalirudin group) or matched placebo (in the heparin plus Gp IIb/IIIa group) included abrupt or side-branch closure, obstructive dissection, new or suspected thrombus, impaired coronary flow, distal embolization, persistent residual stenosis, unplanned stent placement, prolonged ischemia, or other clinical instability. All patients received aspirin; treatment with clopidogrel 300 mg prior to the interventional procedure was strongly encouraged, followed by daily administration of 75 mg for at least 30 days.

End Points

Prospectively defined secondary end points of this trial were death, myocardial infarction, and repeat revascularization procedures at 6 months and mortality at 1 year. Patients were to return for follow-up interview and an electrocardiogram between 150 and 210 days after randomization for assessment of 6-month outcome. Telephone or mail contact was made to determine vital status at or after 365 days. Data were prospectively collected by study coordinators at each site and entered into an Internet-based electronic case-report form; relevant hospital records were obtained for source documentation. An end point in-hospital myocardial infarction was defined by new significant Q waves in 2 or more contiguous electrocardiographic leads or elevation in creatine kinase or its MB isoenzyme greater than or equal to 2 times the upper limit of normal. After hospital discharge, myocardial infarction was defined by the development of new Q waves or by creatine kinase or MB isoenzyme elevation to greater than 2 times the upper limit of normal. A clinical events committee, blinded to study group allocation, adjudicated all myocardial infarctions through 6 months and urgent repeat revascularization procedures through 30 days. Cause of death by 1 year was assessed by an experienced research nurse who was blinded to treatment allocation, using the Medical Dictionary for Regulatory Activities (MedDRA) definitions.
LONG-TERM EFFICACY OF BIVALIRUDIN DURING PCI

**Statistical Analysis**

To be considered complete, 6-month and 1-year follow-up were required to have occurred at least 150 days and 270 days after randomization, respectively. The 6-month database was finalized on August 1, 2003, and the 1-year database on October 23, 2003; 98.2% of randomized patients had at least 150 days and 98.5% had at least 270 days of follow-up (Figure 1). Kaplan-Meier methods were used to estimate 6-month and 1-year event rates, and comparisons between the 2 treatment groups were performed using the log-rank statistic. A multivariable Cox proportional hazards regression model was constructed to identify among all baseline characteristics those parameters that were independent predictors of 1-year mortality; using the sum of coefficients derived from this model, patients were then classified into tertiles of risk for comparison of mortality rates between the randomized treatment groups. Kaplan-Meier and proportional hazards models are both time-to-event analyses, which included all randomized patients according to the intention-to-treat principle censored to the time of last follow-up. Mortality rates among individual subgroups were determined by frequency counts, rather than time-to-event analysis.

![Figure 1. Flow of Patients Through 1 Year of Follow-up](image)

**RESULTS**

Baseline characteristics were balanced and did not differ between the 2 treatment groups (Table 1). Mean age was about 63 years, approximately one quarter of patients were women, and 27% had diabetes mellitus. Acute coronary syndromes (unstable angina within 48 hours or myocardial infarction within the prior 7 days) were the indications for revascularization in 23% of patients. Eptifibatide or abciximab were chosen by the interventional operator for Gp IIb/IIIa blockade in 55% and 45% of patients, respectively.

Ischemic end points at 6 months are summarized in Table 2. There were no significant differences between treatment groups in event rates for any composite or individual end point.

Death rates at 6 months tended to be less frequent in the bivalirudin group by an absolute 0.4% (1.4% heparin vs 1.0% bivalirudin groups, P = .15), a slight widening of the absolute 0.2% difference observed at 30 days (0.4% heparin vs 0.2% bivalirudin, P = .26; Figure 2). Myocardial infarction rates tended to be lower among patients treated with heparin plus Gp IIb/IIIa blockade, with an absolute 0.8% difference, which was due almost exclusively to non–Q-wave (rather than Q-wave) infarctions and accrued entirely within the first 30 days (7.0% vs 6.2%; P = .23; 8.2% heparin vs 7.4% bivalirudin at 6 months, P = .24; Figure 3). Revascularization rates were nearly identical in the 2 treatment groups at 30 days (2.8% heparin vs 2.7% bivalirudin) but by 6 months favored the heparin group by an absolute 0.7% difference; notably, however, the time-to-event curves crossed at multiple times during the follow-up period (Figure 3). The difference in revascularization rates was confined to nonurgent, surgical revascularization procedures.

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*Patients received no blinded study drug due to no percutaneous coronary intervention performed, physician preference, or other reasons; open-label agents were administered to some of these patients. Eleven patients in the heparin group and 14 patients in the bivalirudin group who had been lost to follow-up at the time of finalization of the 6-month database were subsequently contacted and included in the 1-year database.
Adverse events were collected for the first 30 days, and there were no differences between treatment groups.

By 1 year, 72 of 3008 patients (2.46%) in the heparin plus Gp IIb/IIIa inhibitor group and 56 of 2994 patients (1.89%) in the bivalirudin group had died (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.55-1.11; P = .16; Figure 2). The most common cause of death was cardiac (39 in the heparin group, 29 in the bivalirudin), followed by respiratory (10 heparin, 3 bivalirudin), neoplasia (2 heparin, 7 bivalirudin), nervous system (7 heparin, 4 bivalirudin), neoplasia (2 heparin, 7 bivalirudin), nervous system (7 heparin, 4 bivalirudin), and miscellaneous (10 heparin, 12 bivalirudin). Rates of mortality by 1 year trended lower in the bivalirudin group in all prespecified patient subgroups (Figure 4); differences favoring bivalirudin were apparent in subgroups observed to be at high risk of mortality, including those older than 75 years (odds ratio [OR], 0.51; 95% CI, 0.26-0.98), female (OR, 0.72; 95% CI, 0.40-1.30), or who had diabetes mellitus (OR, 0.58; 95% CI, 0.34-1.05).

Multivariate modeling identified 8 baseline variables that were predictive of 1-year mortality (Table 3). Using this proportional hazards model, patients were categorized into tertiles of risk. Mortality rates were 2.5-fold higher in the moderate-risk tertile than in the low-risk tertile, increasing another 5-fold between the moderate-risk and high-risk tertiles. Among low- or moderate-risk patients, death rates were similar in the bivalirudin group vs the heparin plus Gp IIb/IIIa inhibitor group (0.4% vs 0.3%, respectively, for low risk and 1.1% vs 0.8%, respectively, for moderate risk). Among patients at high risk, however, death occurred significantly less frequently with bivalirudin than with heparin plus Gp IIb/IIIa blockade (6.0% vs 3.9%, respectively, P = .047).

### Table 1. Baseline and Treatment Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Heparin Plus Glycoprotein IIb/IIIa (n = 3008)</th>
<th>Bivalirudin (n = 2994)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>63 (11.0)</td>
<td>63 (10.8)</td>
</tr>
<tr>
<td>Weight, mean (SD), kg</td>
<td>87.5 (18.1)</td>
<td>87.3 (18.2)</td>
</tr>
<tr>
<td>Women</td>
<td>779 (25.9)</td>
<td>758 (25.3)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>784 (26.1)</td>
<td>840 (28.1)</td>
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<tr>
<td>Prior myocardial infarction</td>
<td>1085 (36.7)</td>
<td>1099 (37.4)</td>
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<tr>
<td>Prior coronary artery bypass graft surgery</td>
<td>564 (18.8)</td>
<td>538 (18.0)</td>
</tr>
<tr>
<td>Indication for procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable angina ≤48 h</td>
<td>434 (14.7)</td>
<td>421 (14.3)</td>
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<tr>
<td>Unstable angina &gt;48 h</td>
<td>619 (21.0)</td>
<td>599 (20.3)</td>
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<td>Stable angina</td>
<td>722 (24.4)</td>
<td>770 (26.1)</td>
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<tr>
<td>Positive stress test or other</td>
<td>930 (31.5)</td>
<td>912 (30.9)</td>
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<tr>
<td>Stent procedure</td>
<td>2578 (85.7)</td>
<td>2548 (85.1)</td>
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<tr>
<td>Thienopyridine pretreatment</td>
<td>(85.4)</td>
<td>(86.7)</td>
</tr>
<tr>
<td>Thienopyridine after procedure</td>
<td>2748 (91.5)</td>
<td>2748 (91.9)</td>
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<tr>
<td>Planned glycoprotein Ilb/IIa inhibitor use</td>
<td>2902 (96.3)</td>
<td>. . .</td>
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<tr>
<td>Eptifibatide</td>
<td>1605 (53.4)</td>
<td>. . .</td>
</tr>
<tr>
<td>Abciximab</td>
<td>1289 (42.9)</td>
<td>. . .</td>
</tr>
<tr>
<td>Provisional glycoprotein Ilb/IIa inhibitor use</td>
<td>157 (5.2)†</td>
<td>217 (7.2)†</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>. . .</td>
<td>111 (3.7)</td>
</tr>
<tr>
<td>Abciximab</td>
<td>. . .</td>
<td>106 (3.5)</td>
</tr>
<tr>
<td>Placebo</td>
<td>157 (5.2)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

Ellipses indicate not applicable.

*Values expressed as number (percentage) unless otherwise indicated. All percentages are of patients for whom data were available.

†P = .002.
COMMENT

The primary 30-day results of REPLACE-2 demonstrated that bivalirudin with selective use of a Gp IIb/IIIa inhibitor reduces bleeding and provides protection from short-term ischemic events that is not inferior to that of heparin plus planned Gp IIb/IIIa blockade during contemporary PCI. However, a small nonsignificant excess of periprocedural non–Q-wave myocardial infarctions among bivalirudin-treated patients in this trial led some to criticize the conclusion of non-inferiority and question the long-term durability of clinical benefit with this regimen.

This current analysis of REPLACE-2 confirms that the efficacy of bivalirudin in suppressing ischemic complications remains comparable over long-term follow-up with that of heparin plus Gp IIb/IIIa blockade. By 6 months, no significant differences between treatment groups emerged in rates of death, myocardial infarction, or repeat revascularization. A trend toward better survival with bivalirudin developed by 1 year; although this difference in mortality was not statistically significant, the magnitude of possible benefit with bivalirudin was greatest among patients at highest risk of long-term death. These results demonstrate that long-term clinical outcome is comparable with a strategy of bivalirudin and provisional Gp IIb/IIIa blockade vs heparin plus planned Gp IIb/IIIa inhibition. Coupled with the advantages of bivalirudin with regard to reduced hemorrhagic complications, cost savings, and ease of administration, this long-term analysis establishes bivalirudin plus provisional Gp IIb/IIIa inhibition as an attractive antithrombotic strategy for patients undergoing elective or urgent PCI.

Early studies of bivalirudin compared with heparin during PCI suggested that both ischemic and hemorrhagic complications might be reduced by this agent. The primary findings of the REPLACE-2 trial substantiated the efficacy of bivalirudin in contemporary interventional practice, demonstrating that replacement of heparin...
with this direct thrombin inhibitor permits selective rather than universal use of Gp IIb/IIIa inhibitors while maintaining suppression of ischemic events and reducing bleeding and costs. Although 30-day results met formal statistical criteria for noninferiority of bivalirudin compared with heparin plus Gp IIb/IIIa inhibition with respect to the composite ischemic end point, concern was expressed by some physicians regarding the nonsignificant absolute 0.8% excess risk of periprocedural non-Q-wave myocardial infarction in the bivalirudin group (6.6% bivalirudin vs 5.8% heparin, P = .43). Myocardial enzyme elevations during PCI have been correlated with increased late (1-year and beyond) mortality risk, thereby providing compelling rationale for use of enhanced antithrombotic regimens to prevent periprocedural myocardial necrosis. Treatment with at least 1 Gp IIb/IIIa antagonist, abciximab, has been associated with a survival benefit after PCI, and the regimen of heparin plus Gp IIb/IIIa blockade has come to be regarded as a standard for the prevention of complications during these procedures. It was therefore imperative to demonstrate that long-term protection from ischemic events and mortality after PCI is not compromised with a bivalirudin regimen in which Gp IIb/IIIa blockade is used only provisionally.

The 1-year findings of the REPLACE-2 trial presented herein validate the durable efficacy of bivalirudin. Not only was there no excess of mortality with bivalirudin therapy, but death rates actually trended to be better in the bivalirudin group. Moreover, the magnitude of difference favoring bivalirudin appeared greater in high-risk patient subgroups and was independent of the choice of Gp IIb/IIIa inhibitor (abciximab or eptifibatide) or pretreatment with a thienopyridine. Subgroup analyses admittedly may be subject to spurious findings due to dichotomization of patients according to potentially arbitrary subsets; it is for this reason that a multivariable analysis was also performed to identify higher risk patients by integrating the variety of baseline factors that independently contribute to poor long-term outcome. Patients in the highest tertile of risk by that regression analysis showed the largest difference in 1-year mortality rates favoring bivalirudin over heparin plus Gp IIb/IIIa blockade, a difference that reached statistical significance (albeit without correction for multiple comparisons).

We can only speculate why 1-year mortality rates were numerically lower with bivalirudin treatment despite a slight excess of periprocedural myocardial infarctions in that group. Both

Figure 4. One-Year Mortality by Subgroups and Treatment Assignment*

Table 3. Baseline Predictors of Mortality at 1 Year by Multivariate Proportional Hazards Modeling*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, 1 per year</td>
<td>1.05 (1.03-1.07)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>3.10 (2.03-4.73)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline hemoglobin, per 1 mg/dL</td>
<td>0.76 (0.68-0.85)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline serum creatinine, per 1 mg/dL</td>
<td>1.66 (1.20-2.28)</td>
<td>.002</td>
</tr>
<tr>
<td>Body mass index†≤28</td>
<td>0.90 (0.83-0.97)</td>
<td>.004</td>
</tr>
<tr>
<td>&gt;28</td>
<td>1.14 (1.04-1.25)</td>
<td>.006</td>
</tr>
<tr>
<td>Tobacco use in prior year</td>
<td>1.85 (1.18-2.91)</td>
<td>.008</td>
</tr>
<tr>
<td>History of angina</td>
<td>2.02 (1.17-3.48)</td>
<td>.012</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.50 (1.01-2.23)</td>
<td>.046</td>
</tr>
</tbody>
</table>

*ACS indicates acute coronary syndrome; GP, glycoprotein; LMWH, low-molecular-weight heparin.

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of these nonstatistically significant trends may simply have been due to the play of chance. However, the statistically significant reduction in major bleeding events among patients receiving bivalirudin may translate to an advantage that offsets any late consequences of a small excess in early myocardial infarctions. In REPLACE-2, postprocedural bleeding was more strongly correlated with 1-year mortality (OR, 3.5; 95% CI, 1.9-6.5) than was creatine kinase-MB enzyme elevation (OR, 2.6; 95% CI, 1.5-4.5). 17 It cannot yet be concluded that this bivalirudin regimen is superior to heparin plus Gp IIb/IIIa for 1-year mortality on the basis of an overall nonstatistically significant trend in the current REPLACE-2 trial. Nevertheless, the consistent directionality of benefit in this study of more than 6000 patients (the largest yet performed of an acute antithrombotic therapy during PCI) provides convincing evidence that protection against death with bivalirudin is comparable with heparin plus Gp IIb/IIIa blockade, even in high-risk patients for whom Gp IIb/IIIa inhibition would be expected to impart the most clinical benefit. 18

Nonfatal cardiac end points also reflected similar outcomes over 6 months of follow-up with bivalirudin vs heparin plus Gp IIb/IIIa inhibition. Myocardial infarctions tended to occur early following the interventional procedure; thereafter, time-to-event curves (Figure 3) remained parallel, suggesting no differential benefit between these 2 antithrombotic strategies subsequent to a relatively short periprocedural period of maximal risk. Repeat target vessel revascularization rates were nearly identical in the 2 groups at 30 days, diverging nonsignificantly by 6 months in favor of heparin plus Gp IIb/IIIa blockade. This difference was not due to urgent revascularization procedures, arguing against a greater frequency of acute ischemic complications as a precipitating factor among patients treated with bivalirudin. Because neither heparin nor Gp IIb/IIIa blockade has been convincingly shown to reduce restenosis following PCI, it is difficult to postulate a mechanism whereby replacement of these agents with bivalirudin would lead to more frequent need for nonurgent repeat target vessel revascularization (the clinical surrogate for restenosis). The fact that time-to-event curves for revascularization crossed at multiple times over the 6-month period suggests that observed differences in revascularization rates may be due to the play of chance, rather than a consistent influence of either antithrombotic regimen.

The acute and long-term findings of REPLACE-2 cannot be extrapolated to patient groups that were excluded from enrollment in this trial, principally those with unstable ischemic syndromes requiring uninterrupted therapy with Gp IIb/IIIa inhibitors or heparin or those undergoing primary PCI for acute myocardial infarction. Despite exclusion of these patients, however, 30-day and 1-year ischemic event rates in REPLACE-2 were similar to those in other recent PCI trials, 2,3,20 arguing against an assertion that the patient population in REPLACE-2 was “low risk.” Moreover, bivalirudin therapy was associated with favorable 1-year mortality rates among patients in this trial who had been treated with unfractionated or low-molecular-weight heparin but were sufficiently stable to permit discontinuation of the anticoagulants for the specified 6- or 8-hour periods before randomization (Figure 4). The existing body of clinical evidence supports the use of Gp IIb/IIIa inhibitors for patients with unstable ischemic syndromes 21-25 although an ongoing large-scale trial (Acute Catheterization and Urgent Intervention Triage strategY [ACUITY]) is testing the efficacy of bivalirudin with or without Gp IIb/IIIa blockade in these high-risk patients. For all but the relatively select groups of patients not included in the trial, however, the primary and follow-up results of REPLACE-2 validate the effectiveness and safety of bivalirudin with provisional Gp IIb/IIIa blockade during contemporary PCI.
REFERENCES


