One-Year Results of the Thrombolysis in Myocardial Infarction Investigation (TIMI) Phase II Trial

David O. Williams, MD; Eugene Braunwald, MD; Genell Knatterud, MD; Joseph Babb, MD; John Bresnahan, MD; Mark A. Greenberg, MD; Albert Raizner, MD; Alan Wasserman, MD; Thomas Robertson, MD; Richard Ross, MSc; and TIMI Investigators

**Background.** The Thrombolysis in Myocardial Infarction (TIMI) Phase II Trial randomized 3,339 patients to either an invasive (INV, n=1,681) or a conservative (CON, n=1,658) strategy after intravenous recombinant tissue-type plasminogen activator (rt-PA) for acute myocardial infarction.

**Methods and Results.** The patients assigned to the INV strategy routinely underwent cardiac catheterization, and when anatomically appropriate, percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting 18–48 hours after infarction. CON patients had these procedures only in response to the occurrence of spontaneous or provoked ischemia. One-year follow-up data are available in 3,316 patients (99.3%). The primary trial end point, death and nonfatal reinfarction, occurred in 14.7% of INV patients and in 15.2% of CON patients (p=NS). When analyzed individually, there was no difference (p=NS) in death (INV, 6.9%; CON, 7.4%) or recurrent infarction (INV, 9.4%; CON, 9.8%) between the two groups. Anginal status at 1 year was also similar. Cardiac catheterization and PTCA were performed more often in INV (98.0% and 61.2%, respectively) compared with CON (45.2% and 20.5%, respectively) patients. At 1 year, the cumulative number of patients who underwent coronary bypass surgery (INV, 17.5%; CON, 17.3%) was similar in the two groups.

**Conclusions.** The INV and CON strategies resulted in similar favorable outcomes at 1 year of follow-up. In particular, the rates of mortality and reinfarction were not different and were impressively low in both groups. One possible advantage of the INV strategy was detected in subgroup analyses. In patients with a history of myocardial infarction, the data are suggestive that 1-year mortality was lower in INV patients (10.3%) than in CON patients (17.0%) (p=0.03). (Circulation 1992;85:533–542)

The Thrombolysis in Myocardial Infarction (TIMI) Phase II Trial is a randomized multicenter clinical investigation that was designed to compare two management strategies for patients with acute myocardial infarction (AMI) treated with thrombolytic therapy. The invasive strategy (INV) involved the routine performance of cardiac catheterization and coronary revascularization by means of percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting (CABG). The conservative strategy (CON) used catheterization and revascularization only when prompted by episodes of spontaneous or provoked ischemia. At 6 weeks of follow-up, there was no apparent benefit of one strategy over the other when judged according to the occurrence of certain important clinical end points including death, nonfatal reinfarction, and the extent of left ventricular dysfunction. Because the potential benefits of one strategy, however, might not be detected within 6 weeks after AMI, TIMI II patients have been followed in an effort to determine whether differences in outcome, based on initial strategy assignment, might become evident. Accordingly, the purpose of this report is to provide information on all patients randomized and to describe the results of the TIMI II Trial at 1 year of follow-up. The specific aims are to determine the incidence of certain clinical events...
and the chronology of these events in the randomized cohort and to analyze outcome for selected clinical subgroups.

See p 839

Methods
Details of the TIMI II Trial have been described previously. In brief, consenting patients <76 years of age with greater than 30 minutes of chest pain characteristic of myocardial ischemia, diagnostic electrocardiographic ST segment elevation, presentation within 4 hours of pain onset, and no contraindications to thrombolytic therapy received a 6-hour infusion of recombinant tissue-type plasminogen activator (rt-PA) alteplase, (Activase®) and were randomly assigned to either the INV or CON strategies. Patients also received heparin and aspirin. Those assigned to the INV strategy underwent routine cardiac catheterization including left ventricular and coronary cineangiography within 18–48 hours of randomization and PTCA if catheterization findings demonstrated appropriate anatomy. Aspirin was part of recommended study treatment for all invasive strategy patients before PTCA. CABG was recommended for INV patients if coronary anatomy was too complex or hazardous for PTCA. Patients assigned to the CON strategy underwent procedures only in response to either spontaneous or provoked myocardial ischemia. Patients eligible for enrollment in the trial of β-blocker therapy (TIMI II B), were randomized to either the immediate or delayed administration of metoprolol. One-year results were presented previously and will not be discussed.

Research nurse coordinators from each participating clinical site were trained, tested, and certified in the performance of collection, recording, and transfer of data to the coordinating center. For each patient, outcome was determined at the time of hospital discharge, 6 weeks after enrollment, and at 1 year from the time of recruitment. Patient status was determined by formal clinic visit at 6 weeks and 1 year and by telephone contact at 3 and 6 months. Compilation, editing, and analysis of data were performed by the coordinating center.

End Points
In TIMI II, the primary end point for comparing the invasive and conservative strategies was survival free of recurrent myocardial infarction at 42 days. The present analysis extends the TIMI II results in a secondary analysis to 1 year of follow-up.

In this analysis, survival data are based on all-cause mortality, including fatal myocardial infarction. Patients were also monitored for clinical events including myocardial ischemia. Recurrent chest pain in the hospital refers to chest pain that occurred with or without myocardial infarction at least 18 hours after study entry but during the hospital stay. Severe ischemic event in patients after discharge refers to chest pain occurring with or without myocardial infarction for which the patient was admitted to the hospital. Myocardial infarction was diagnosed when the patient had prolonged chest pain with characteristic electrocardiographic changes and/or confirmatory cardiac enzymes. Events reported by the research nurse coordinators were classified by the Mortality and Morbidity Classification Committee. Members of this committee were cardiologists who were not TIMI clinical center investigators; events were classified without knowledge of treatment assignment and according to criteria established before the classification of these events began. The Mortality and Morbidity Classification Committee reviewed and classified all reported myocardial infarction events. The classification criteria were different for events within 18 hours from study entry to allow only new events to be classified as reinfarction. In this analysis, reinfarction data are based on all new myocardial infarction after the qualifying infarction and including new, fatal myocardial infarctions.

Strokes include all events since randomization, both during the initial hospitalization and after the initial hospitalization. Only neurological events occurring during the initial hospitalization were reviewed by two neurologists who were not TIMI clinical center investigators and have been described in detail.

Statistical Methods
For discrete data variables, comparisons of proportions of patients having the given attribute were made with a χ² test. For continuous data variables, comparisons of mean values were made with a two-tailed Student's t test. Cumulative event rates were estimated using the product-limit (Kaplan-Meier) method and comparisons in the event distributions over time were made using the log-rank statistic. These analyses were performed using Statistical Analysis System (SAS) programs. All analyses are based on a data file (including all follow-up information) established January 1991. To adjust for multiple testing, a value of p<0.01 was specified as indicating statistical significance for the treatment comparisons with respect to the primary end point (combined mortality and reinfarction 6 weeks after thrombolytic therapy). For comparisons of other end points, probability values between 0.01 and 0.001 provide some evidence of differences between treatments, and probability values <0.001 provide strong evidence of such differences. All tests of differences were planned as two-tailed tests in the TIMI II design.

The effects of treatment strategy, selected baseline characteristic, and the interaction of treatment strategy and baseline characteristic were evaluated using a Cox proportional hazards regression model. A test of the hypothesis that the interaction effect is zero was performed to determine whether the difference in events between the two treatment strategies was the same for patients with and without the characteristic. Cox regression models were also used to estimate relative risks and confidence intervals for
1-year end points. These analyses were performed using BioMedical Data Package (BMDF) programs.

**Results**

The preliminary report on the first 6 weeks of follow-up was based on data for patients recruited before June 5, 1988, or 3,162 of the 3,339 enrolled at the end of recruitment. As before, there were no important differences between the 1,681 assigned to the INV strategy and the 1,658 assigned to the CON strategy (Table 1). Patients in both strategies were for the most part men who were experiencing their first myocardial infarction, <70 years of age, and approximately two thirds had at least one clinical characteristic indicative of increased risk for infarct-related mortality. Approximately half had anterior wall infarction.

The vital status of all patients 6 weeks after entry was known; however, three patients in the invasive strategy and three patients in the conservative strategy could not be contacted after hospital discharge to obtain information on nonfatal events. Thus, the follow-up for nonfatal events at 6 weeks was available for 99.8% of patients in both strategies.

At 1 year, the vital status of 11 patients in the invasive group and 12 in the conservative group could not be ascertained. Accordingly, follow-up for mortality was complete for 99.3% of patients in both strategies. A small number of patients for whom vital status was known did not have complete information on nonfatal events available (19 in the invasive group and 16 patients in the conservative group). Thus, follow-up for nonfatal events at 1 year was 98.2% and 98.3% in the invasive and conservative strategies, respectively.

**Comparison of Randomized Cohorts**

The primary response variable for the TIMI II Trial was the combined end point of death and nonfatal reinfarction. From time of enrollment to 52 weeks, there was no difference between INV and CON patients in the incidence of death and reinfarction (Table 2). The relative risk of the combined end point for invasive strategy patients compared with conservative strategy was 0.98 (99% confidence interval, 0.78–1.24). When analyzed as individual end points, the incidence of death and of AMI were impressively low for both groups at 1 year and were not significantly different. The 1-year cumulative mortality in the INV group was 6.9% and for the CON patients it was 7.4% (relative risk, 0.93; 99% confidence interval, 0.67–1.30). The cumulative incidence of recurrent AMI at 1 year was 9.4% and 9.8%, respectively (relative risk, 0.97; 99% confidence interval, 0.73–1.30).

Similar patterns were noted for death and reinfarction in the two groups (Figures 1–3). Most events occurred within 6 weeks after the infarction that qualified the patient for TIMI. For the INV patients, most events occurred during hospitalization. Early during hospitalization, reinfarction was more common in INV patients (p=0.005 through 1 week).

At the 1-year follow-up visit, there was no difference in the proportion of patients experiencing angina or in the severity of angina based on the Canadian Cardiovascular Society Angina Classification System. During the first year of follow-up, however, more patients in the CON group were rehospitalized for angina than in the INV group (19.6%
versus 14.7%, respectively; \( p<0.001 \)). Similarly, rehospitalization for cardiac reasons was observed more commonly in CON patients (38.1%) than in INV patients (29.6%, \( p<0.001 \)). There was no difference in the total days of rehospitalization between the two groups. The incidence of stroke during follow-up in the two groups was the same (2.0%) at 1 year.
TABLE 2. Continued.

<table>
<thead>
<tr>
<th>Canadian heart angina class</th>
<th>Invasive (n=1,681)</th>
<th>Conservative (n=1,658)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Six weeks</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with follow-up visit</td>
<td>1,436</td>
<td>85.4</td>
</tr>
<tr>
<td><strong>Canadian Cardiovascular Society Angina class†</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class 0</td>
<td>1,123</td>
<td>78.2</td>
</tr>
<tr>
<td>Class I</td>
<td>198</td>
<td>13.8</td>
</tr>
<tr>
<td>Class II</td>
<td>80</td>
<td>5.6</td>
</tr>
<tr>
<td>Class III</td>
<td>25</td>
<td>1.7</td>
</tr>
<tr>
<td>Class IV</td>
<td>10</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>One year</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with follow-up visit</td>
<td>1,285</td>
<td>76.4</td>
</tr>
<tr>
<td><strong>Canadian Cardiovascular Society Angina class†</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class 0</td>
<td>969</td>
<td>75.5</td>
</tr>
<tr>
<td>Class I</td>
<td>196</td>
<td>15.3</td>
</tr>
<tr>
<td>Class II</td>
<td>86</td>
<td>6.7</td>
</tr>
<tr>
<td>Class III</td>
<td>23</td>
<td>1.0</td>
</tr>
<tr>
<td>Class IV</td>
<td>10</td>
<td>0.8</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass grafting.

*Patients requiring catheterization in the conservative strategy.
†Denominators for these percentages are the numbers of patients with follow-up visits.

As expected from the trial design, early (within 21 days) cardiac catheterization was performed in nearly all (97.2%) INV patients and less commonly (27.5%, p<0.001) in CON patients. Only 0.9% of additional INV patients underwent cardiac catheterization during 1 year of follow-up in contrast to the CON cohort in whom the cumulative incidence of cardiac catheterization by 1 year had increased to 45.2%. Second catheterizations were performed in 24.9% of INV patients and in 25.8% of CON patients within 1 year after study entry (p=0.65). In the conservative strategy, those patients who developed myocardial ischemia spontaneously or during exercise testing or had reinfarction or hemodynamic deterioration were to undergo catheterization and revascularization if the anatomy was suitable.

Study protocol called for PTCA to be performed if the coronary anatomy was suitable early during hospitalization for patients assigned to INV strategy. Through the first 3 weeks after entry (Table 2), PTCA was performed in 60.2% of INV patients compared with 12.5% of CON patients (p<0.001). By 6 and 52 weeks, respectively, 14.2% and 20.5% of CON patients had undergone PTCA, whereas only 1% of additional INV patients underwent the procedure. Thus, PTCA was performed much more fre-
CUMULATIVE RATES OF REINFARCTION THROUGH ONE YEAR
TIMI II

PERCENT

20
15
10
5
0

WEEKS AFTER STUDY ENTRY

0
6
12
18
24
30
36
42
48
54
60
66
72

Figure 3. Graph of cumulative Kaplan-Meier event rates for reinfarction according to strategy assignment from entry through 52 weeks.

Quently in the INV patients, almost five times as much during the period of initial hospitalization. Periprocedural (within 24 hours) mortality for PTCA in the INV group was 0.6%, with a reinfarction rate of 4.5%. The number of CON patients undergoing PTCA from 6 weeks to 1 year was small (6.3%). More patients in the INV group had CABG by 3 weeks (11.6%) than in the CON group (9.1%, p=0.01). At 6 weeks and at 1 year, the cumulative number of patients who received CABG was similar in the two groups (CON, 11.5% and 17.3%; INV, 12.7% and 17.5%, respectively).

Of the 972 INV patients who had PTCA during the first 6 weeks from enrollment and survived to 6 weeks, 104 (10.8%) had an additional revascularization procedure within the 1-year follow-up. A second PTCA was performed in 66 (6.8%), whereas 46 (4.8%) had CABG, of which eight had both procedures. Of 224 CON patients who had PTCA within 6 weeks, a second PTCA was performed in 18 (8.1%), whereas CABG was carried out in 12 (5.4%) during follow-up. There was no difference in the proportion of INV versus CON patients who required a second revascularization procedure.

Nonrandomized Subset Analysis

The cumulative 1-year event rates for death and reinfarction were analyzed in various subsets of INV and CON patients. There was no difference in the occurrence of death or reinfarction between INV and CON strategy patients when analyzed in terms of sex, age greater or less than 70 years, anterior or nonanterior infarction location, time to t-PA therapy greater or less than 2 hours, low-risk or not-low-risk class, presence or absence of shock, catheterization performed or not performed during hospitalization, or CABG performed or not performed during hospitalization.

A difference in outcome was noted between patients with and without prior myocardial infarction at 42 days (interaction, p=0.004) but was not as strong at 1 year (interaction, p=0.03). Patients with a history of AMI assigned to the INV strategy had a lower 42-day mortality (6.0%) compared with those assigned to the CON strategy (11.5%, p=0.04). One-year mortality in patients with prior AMI was 10.3% and 17.0% in the INV and CON groups, respectively (p=0.03). These suggestive differences were not changed by analyses to adjust for other baseline characteristics. Revascularization by either PTCA or CABG was performed in 74.8% of patients with prior AMI assigned to the INV strategy compared with 41.0% of those in the CON group.

Discussion

Considerable effort was devoted to the planning of TIMI II so that it would be directly applicable to clinical practice in managing patients with AMI. TIMI II was a trial designed to compare two treatment strategies rather than a specific therapy or intervention. The assigned strategies were implemented early in the patient's course, similar to the clinical setting wherein a plan for subsequent hospital care for an AMI patient begins immediately following presentation.

The invasive strategy was developed on the presumption that thrombolytic therapy may be effective in establishing reperfusion but could leave uncorrected a severe residual atherosclerotic narrowing of the coronary artery responsible for the infarction. This "partially treated" condition could render the patient susceptible to reinfarction because of early reclosure of the coronary artery or recurrent ischemia related to persistent significant partial obstruction.9,10 PTCA after thrombolytic therapy offered the potential benefit of relieving residual atherosclerotic narrowing11 and thus reducing the likelihood of recurrent ischemia-related events.

To provide PTCA the greatest opportunity to demonstrate efficacy and safety after thrombolytic therapy, this procedure was performed only when coronary anatomy was suitable for PTCA as judged by the results of cardiac catheterization and angiography. Accordingly, patients with patent yet significantly stenosed infarct arteries with coronary anatomic characteristics that did not preclude PTCA were selected for the procedure. Such patients could be considered as those who might receive the greatest benefit from the procedure because they had achieved reperfusion but had severe residual coronary narrowing. Patients with coronary anatomy known to be associated with an increased risk of PTCA related untoward events, for example, left main disease or its equivalent, were excluded and referred for CABG.12,13 In addition, patients with totally occluded arteries at 18–48 hours did not undergo PTCA unless recurrent ischemia had occurred. Not performing a PTCA in such patients reduced the chance of a PTCA-related adverse event in patients in whom the likelihood of benefit from PTCA is low. Thus, by design, PTCA was not performed in each patient assigned to the INV strategy.
but rather in those in whom the greatest potential benefit was anticipated.

The 1-year mortality of the INV and CON groups was not significantly different. Thus, the INV strategy did not enhance survival in an important way in comparison with the CON strategy. However, the mortality rates of the INV and CON groups were both low. Hence, the similarity between INV and CON patients was not attributable to INV patients failing worse than expected; rather, the CON patients did well. In fact, the 1-year mortality rate (7.4%) of CON patients was lower than that previously reported in other studies of patients treated with intravenous t-PA (10.5%).14 streptokinase (10.5–17.2%),14–16 or anisoylated plasminogen streptokinase activator complex (10.8%).17 Although substantial differences between TIMI II and these other trials exist, none of the other trials incorporated the standardized use of cardiac catheterization, PTCA, or surgery, an integral component of the CON strategy in TIMI II. The favorable results of the TIMI II CON group could not be attributed to the selection of less-ill patients because 67% of patients had features of increased risk and patients with pulmonary edema or cardiogenic shock were not excluded.1 The rates of reinfarction and death or reinfarction at 1 year were also similar in both groups. With 1,650 patients in each group, there would be 80% power to detect a clinically important reduction of 27% or more in event rates when the higher rate was 15% ($\alpha$ = 0.01 by two-sided test).

Early during hospitalization, reinfarction was more common in the INV group. Although not statistically different, the rate of reinfarction in the CON group was slightly higher at 1 year (9.8% versus 9.4%) in comparison with the INV group. Because reinfarction was more frequent in the INV group during the early period but the cumulative rate was lower at 1 year, one might speculate that the rate at which reinfarction occurred over the course of 1 year might in fact be lower in the INV group compared with the CON group. The observed incidence of reinfarction from 6 weeks to 1 year in the INV group was 2.9% and in the CON group 3.3% ($p$ = NS). Of additional note is that because the reinfarction rate in the INV group occurred early during the hospitalization, it may have been associated with procedural aspects of acute cardiac catheterization and PTCA. Should further technological advances reduce the incidence of complications associated with these procedures, true benefit in reducing the incidence of reinfarction in the INV arm might become evident.

For patients assigned to the CON strategy, the incidence of death or recurrent AMI beyond 6 weeks was low. This observation is of particular interest in respect to the CON group because the majority of patients (72.5%) did not undergo either in-hospital cardiac catheterization or revascularization. Had the CON strategy been inadequate in identifying appropriate patients for revascularization, one might have expected an increased incidence of events beyond 6 weeks. The low rate of late events suggests that using the occurrence of spontaneous or provokable ischemia as an indication for more aggressive evaluation is a reasonable screening mechanism to identify patients at increased risk for recurrent infarction. Follow-up beyond 1 year will be helpful in confirming these results.

In the INV group, PTCA was performed in about 60% of patients during the hospitalization and in a few additional patients thereafter. It was expected that all patients would not undergo in-hospital PTCA. This procedure is acknowledged as not being applicable to all patients with coronary disease, and there are situations in which PTCA is clearly known to be hazardous. In fact, application of PTCA routinely to patients with AMI has been associated with a mortality in excess of that after thrombolytic therapy alone.18

In comparison with the INV group, PTCA was performed in only 12.5% of CON patients within 2 weeks and 14.2% by 6 weeks, substantially less than that of the INV group. Additional PTCA beyond 6 weeks was performed in only 6.3% of CON patients. By design, some use of PTCA was anticipated in the CON group because the protocol called for this procedure to be performed in response to evidence of ischemia. Nevertheless, there was nearly a threefold difference at 1 year in the use of PTCA in INV compared with CON groups. From these observations, for the types of patients studied in TIMI II and for the dose regimen of t-PA used, one out of seven patients will need PTCA before hospital discharge. Although there are many more patients in whom PTCA could be done, performing the procedure in such patients appears to offer no additional benefit.

PTCA after 21 days was performed more often in patients in the CON group than in the INV group. This small but significant difference in additional procedures may have been in response to episodes of late ischemia because more CON patients (19.6%) than INV patients (14.7%) were rehospitalized for angina during the 1-year follow-up. This explanation may also apply for the 8.2% of additional patients in the CON group who underwent CABG from 21 days to 1 year.

Regardless of initial strategy assignment, most (76%) TIMI II patients did not report angina pectoris at the 1-year visit. Only 2.6% of the INV and 1.8% of the CON groups had severe (Canadian class III or IV) angina. These results are similar to prior observational data in which PTCA was performed in coronary disease patients with angina as an indication. The recent NHLBI Registry described an incidence of freedom from angina at 1 year of 76%.19

TIMI II was designed to test the hypothesis that an aggressive strategy was superior to a more conservative one in patients treated with intravenous rt-PA in the early hours of AMI. Superiority of the INV strategy was not detected for the large cohort of patients studied. Because it is conceivable, however, that a certain subset of AMI patients could benefit
from a more aggressive approach, additional “hypothesis-generating” analyses of selected subgroups were performed. For nearly all characteristics evaluated, no differences in outcome were observed between INV and CON groups.

However, a lower 6-week mortality that was not as marked at 1 year was observed in INV versus CON for patients with a history of myocardial infarction. This finding cannot be ascribed to features of the trial design and may reflect a true treatment effect of the INV strategy. A definitive explanation of why such patients would benefit from an INV approach cannot be derived from the data base of this trial. On protocol angiography, INV patients with prior myocardial infarction did have a greater prevalence of multivessel disease than INV patients without prior myocardial infarction (60.2% versus 28.3%, respectively, p<0.001). Also for INV patients, the left ventricular function was more compromised in those with prior myocardial infarction than without (mean ejection fractions of 42.1% and 48.3%, respectively; p<0.001). Routine PTCA in such a group could be beneficial because surgical revascularization has been shown to enhance survival in patients with advanced coronary artery disease, particularly in those with impaired left ventricular function.20–22 Although no trial has yet demonstrated that PTCA can enhance survival in comparison with medical therapy, PTCA is acknowledged as a very potent and effective alternative means of relieving coronary narrowing and normalizing coronary circulatory dynamics. Offering routine revascularization to patients with more advanced disease may prove to be valuable after rt-PA for AMI. It is important to note, however, the limitations of retrospective subset analysis. At best, these data suggest that a benefit of routine PTCA in patients with prior AMI may exist. Additional investigation is required to confirm whether this hypothesis is correct.

Conclusions

INV and CON strategies after intravenous t-PA in AMI result in similar favorable 1-year outcomes. The favorable outcome of the CON group was achieved without excessive late PTCA or CABG and is indicative of a rather stable patient population. The initial conclusion of TIMI II, namely that an INV strategy assessed in terms of mortality and reinfarction is not superior to a CON strategy, remains valid.

Appendix

Participants in the TIMI Phase II Trial

Study chairman: E. Braunwald, MD, Harvard University, Boston. Coordinating center: Maryland Medical Research Institute, Baltimore (principal investigator: G.L. Knatterud, PhD; coinvestigators: M.L. Terrin, MD, MPH; S. Forman, MA; D.T. Harris; R. Ross, MSc; P.C. Wilkins, BS; M. Frederick, PhD; P.L. Canner, PhD; M. Carroll; J. Depkin, BS; J. Dotson; C. Fiery; M. Johnson; C. Kelly; P. Noble, BS; B. Thompson, PhD; W.R. Bell, MD; and L. Scherlis, MD). Radiographic core laboratory: University of Washington, Seattle (principal investigator: H.T. Dodge, MD; coinvestigators: B.G. Brown, MD, PhD; J.W. Kennedy, MD; F.H. Sheehan, MD; B. Bisson; and E. Bolson, MS). Radionuclide core laboratory: Yale University, New Haven, Conn. (principal investigator: B. Zaret, MD; coinvestigator: F. Wackers, MD; D.S. Kayden, MD; K. Davis, RTNM; and R. Green, RTNM). Coagulation core laboratory: University of Vermont, Burlington (principal investigator: K. Mann, PhD; coinvestigators: D. Stump, MD; D. Collen, MD; E. Bovill, MD; and R. Tracy, PhD). Electrocardiographic core laboratory for qualifying electrocardiograms: George Washington University, Washington, DC (principal investigator: A.M. Ross, MD; coinvestigators: G.B. Bren, MD; and A.G. Wasserman, MD). Electrocardiographic core laboratory for exercise electrocardiograms: St. Louis University, St. Louis, Mo. (principal investigator: B.R. Chaitman, MD; coinvestigators: R.D. Wiens, MD; L. Shaw, MS; M. Haueisen, BS; and L.T. Younis, MD, PhD). National Heart, Lung, and Blood Institute Program Office: National Institutes of Health, Bethesda, Md. (principal investigator: E.R. Passamani, MD; coinvestigators: T.L. Robertson, MD; G. Lan, PhD; R. Solomon, MHS; and G. Sopko, MD). Pathology core laboratory: National Institutes of Health, the Clinical Center, Bethesda, Md. (principal investigator: W.C. Roberts, MD; coinvestigator: J. Kalan, MD). Percutaneous transluminal coronary angioplasty quality control laboratory: Brown University, Providence, R.I. (principal investigator: D.O. Williams, MD; coinvestigators: R. Riley, MD; H. White, MD; B. Sharaf, MD; F. Fedele, MD; E. Thomas, MD; T. Drew, MD; J. Joelson, MD; and D. Hardink, RN). Drug distribution center: Cooperative Studies Program, Veterans Administration Medical Research Service, Albuquerque, N.M. (principal investigator: C. Colling, RPh, MD; coinvestigators: C. Haakenson, RPh, MS; and M. Sather, RPh, MS).

Clinical Centers

Albert Einstein College of Medicine–Montefiore Medical Center, New York (principal investigator: H.S. Mueller, MD; coinvestigators: M.A. Greenberg, MD; R. Grose, MD; G. Gordon, MD; J.D. Goldfischer, MD; M. Bensman, MD; J. Cooper, MD; B. Ventura, RN; K. Hemingway, RN; M. Stein, RN; P. Michaud-Edelstein, RN; L. Henson, RN; J. Durkin, RN; and P. Murphy, RN); Baylor College of Medicine, Houston, Tex. (principal investigator: R. Roberts, MD; coinvestigators: P. Nelson, RN; S. Minor, MD; C. Pratt, MD; A. Raizner, MD; W.L. Winters, MD; M.S. Verani, MD; J.M. Lewis, MD; J. Heibig, MD; N. Kleinman, MD; and M.K. VanderMolen, RN); Baystate Medical Center, Springfield, Mass. (principal investigator: M.J. Schweiger, MD; coinvestigators: R.E. Gianelly, MD; T. Marantz, MD; M. Porway, MD; E. Brickman, RN; F. Blank, RN; and J. Mitchell, RN); Boston University Medical Center,
Boston (principal investigator: T.J. Ryan, MD; coinvestigators: C.S. Apstein, MD; J.B. Cadigan III, MD; D.P. Faxon, MD; A.K. Jacobs, MD; M.A. Kellett Jr., MD; B.J. Polansky, MD; N.A. Ruocco, MD; T.A. Sanborn, MD; T. Varricchioz, RRT; D.A. Weiner, MD; N. Battinelli, RN; and B. Hankin, RN); Bridgeport Hospital, Bridgeport, Conn. (principal investigator: J.D. Babb, MD; coinvestigators: Z.A. Adefuin, MD; M. Driesman, MD; J. Meizlish, MD; and D. Yasick, RN); Brown University, Providence, R.I. (principal investigator: D.O. Williams, MD; coinvestigators: T.M. Drew, MD; R.S. Riley, MD; H.J. White, MD; D. Shefchyk, MD; J. Joelson, MD; E. Thomas, MD; B. Sharaf, MD; F. Fedele, MD; M. Nathanson, MD; G. McKendall, MD; D. Becker, MD; D.L. Hardink, RN; M. Macedo, RN; G. Weeks, MD; R. Mich, MD; and E. Berger, MD); Columbia University, New York (principal investigator: E. Powers, MD; coinvestigators: A. Berke, MD; L. Johnson, MD; A.B. Nichols, MD; D.S. Reiton, MD; A. Schwartz, MD; R. Watson, MD; E. Escala, RN; H.S. Wasserman, MD; and M. Apfelbaum, MD); Cornell Medical Center, New York (principal investigators: J.S. Borer, MD; and T.L. Schreiber, MD; coinvestigators: D.H. Miller, MD; J.W. Moses, MD; I. Tamari, MD; B. Charash, MD; B. Gerling, MD; D.A. Silvasi, RN; and A. McNulty, RN); George Washington University, Washington, DC (principal investigator: A.M. Ross, MD; coinvestigators: G.B. Bren, MD; R.I. Katz, MD; R.H. Leiboff, MD; P.J. Varghese, MD; A.G. Wasserman, MD; M. Magee, RN; G. Carvallo, RN; J. Mendelson, RN); Harvard University, Boston (principal investigator: D.S. Baik, MD; coinvestigators: D. Diver, MD; S. Herson, MD; J.E. Markis, MD; R.G. McKay, MD; B. Lorell, MD; C. (Brewer) Senerchia, RN, MS; G.A. Carey, RN; and J. Schweiger, RN); Maine Medical Center, Portland (principal investigator: C.T. Lambare, MD; coinvestigators: W.D. Alpern, MD; R.A. Anderson, MD; D.J. Cutler, MD; J.P. Driscoll, MD; M. Kellett, MD; J.C. Love, MD; P.R. Minton, MD; R.L. Morse, MD; P.K. Shaw, MD; P.W. Sweeney, MD; S. Vermilya, RN; P. Birmingham, RN; and N. McIntire, RN); Mayo Foundation, Rochester, Minn. (principal investigator: J.H. Chesebro, MD; coinvestigators: D.R. Bresnahan, MD; B.J. Gersh, MD; F.A. Miller, MD; M.B. Mock, MD; H.C. Smith, MD; R. Frye, MD; D.L. Hayes, MD; I. Clements, MD; W.K. Freeman, MD; J.A. Rumberger, MD; R. Gibbons, MD; R. Nishimura, MD; R. Rodeheffer, MD; R. Click, MD; J. Oh, MD; L. Sinak, MD; D. Klees, LPN; L. Meyers, LPN; R. Vlietstra, MD; J. Bresnahan, MD; D. Holmes Jr., MD; and G. Reeder, MD); New York Medical College, Valhalla, N.Y. (principal investigator: M.V. Herman, MD; coinvestigators: M.B. Weiss, MD; M. Cohen, MD; J. Levy, MD; M. Feld, MD; R. Grief, MD; J.H. Stein, MD; R. Wallach, MD; A.M. Kanakaraj, RN; V. Rosal-Greif, RN; and Y. Sait, PA); New York University, New York (principal investigator: F. Feit, MD; coinvestigators: J.N. Slater, MD; A. Simon, RN; J. Breed, RN; M.S. Nachamie, MD; W.J. Cole, MD; I.C. Schulman, MD; M.J. Rey, MD; M. Attubato, MD; and S. Shapiro, RN); North Shore University, Manhasset, N.Y. (principal investigator: J. Morrison, MD; coinvestigators: V. Padmananah, MD; P. Reiser, MD; L. Ong, MD; S. Green, MD; A. Tortolani, MD; M.L. Andrezen, RN; T. Imhof, RN; L. Genovese, RN; and M. Ward, RN); Northwestern University, Evanston, Ill. (principal investigator: R. Davison, MD; coinvestigators: T. McDonough, MD; B. Kramer, MD; S. Meyers, MD; P. Niemyski, RN; M. Parker, RN; K. Kaplan, MD; D. Fintel, MD; M. Salinger, MD; D.C. Hueter, MD; G. Wilner, MD; C. Berkowitz, MD; and K. Duun, RN); St. Louis University, St. Louis, Mo. (principal investigator: B.R. Chaitman, MD; coinvestigators: M.G. Vandormael, MD; M.J. Kern, MD; W.P. Hamilton, MD; J.G. Dwyer, MD; T. Thornton, RN; J. Anthony, RN; K. Galan, RN; M. Major, RN; and G. Huber, RN); University of Alabama, Birmingham (principal investigator: W.J. Rogers, MD; coinvestigators: J.G. Arciniegas, MD; W.A. Baxley, MD; R.C. Bourge, MD; T.M. Bulle, MD; T.B. Cooper, MD; L.S. Dean, MD; R. Hess, DO; W.A.H. MacLean, MD; S.E. Papapietro, MD; C. Saenz, MD; A.W.H. Stanley, MD; M.T. Simpson, MD; K. Bynum, RN; T. Eubanks, RN; and L. Maske, RN); University of Massachusetts, Worcester (principal investigator: J. Gore, MD; coinvestigators: J.S. Alpert, MD; J.R. Benotti, MD; J. Leppo, MD; I.S. Ockene, MD; J.F. Rippe, MD; B.H. Weiner, MD; J. Dalen, MD; J.M.J. Gaca, MD; S.P. Ball, RN; J. Corraro, RN; and C. Mahan, RN); University of Minnesota, Minneapolis (principal investigator: M. Hodges, MD; coinvestigators: W.T. Hession, MD; S.W. Sharkey, MD; D. Wysham, MD; I. Goldenberg, MD; A. Adicoff, MD; R. Brandenburg Jr., MD; F.L. Gobel, MD; L. Nordstrom, MD; R. Van Tassel, MD; C. White, MD; R. Wilson, MD; A. Ettinger, RN; L. Palquist, RN; C. Siebold, RN; N. Carruthers, RN; and C. Farmer, RN); University of Texas, Dallas (principal investigator: J. Willerson, MD; coinvestigators: L.D. Hills, MD; G.J. Dehmer, MD; D.L. Brown, MD; M. Winniford, MD; B.G. Firth, MD; M.M. Carry, MD; B. Toates, RN; S. Cochran, RN; P. Surratt, RN; and J. Moore, RN, MSN); Washington University, St. Louis, Mo. (principal investigator: P.A. Ludbrook, MD; coinvestigators: A.J. Tifenbrunn, MD; N.A. Ricciotti, RN, MSN; A.S. Jaffe, MD; and B.E. Sobel, MD); William Beaumont Hospital, Royal Oak, Mich. (principal investigator: R. Ramos, MD; coinvestigators: G. Timmis, MD; V. Gangadharan, MD; S. Gordon, MD; C. Tollis, RN; and E. Worden, RN); Yale University, New Haven, Conn. (principal investigator: L.S. Cohen, MD; coinvestigators: C.K. Francis, MD; J. Alexander, MD; D. Copen, MD; M. Cleman, MD; H. Cabin, MD; M. Remetz, MD; L. Decklebaum, MD; J. Gerard-Amatruda, RN; D. Penn, RN; A. Miller, RN; and C. Piselli, RN).

**TIMI Phase II Committees**

Operations committee: E. Braunwald, MD (chairman), G. Knatterud, PhD; E. Passamani, MD; T.
Robertson, MD; and R. Solomon, MHS; Executive committee: E. Braunwald, MD (chairman); B. Chaitman, MD; J. Chesebro, MD; H. Dodge, MD; G. Knatterud, PhD; K. Mann, PhD; H. Mueller, MD; E. Passamani, MD; R. Roberts, MD; W. Rogers, MD; B. Sobel, MD; D. Stump, MD; D.O. Williams, MD; and B. Zaret, MD; Hemorrhagic event review committee: J. Chesebro, MD (chairman); A. Berke, MD; E. Bovill, MD; F. Feit, MD; J. Gore, MD; L.D. Hillis, MD; C. Lambrew, MD; R. Leiboff, MD; J. Markis, MD; L. Offen, MD; C. Pratt, MD; S. Sharkey, MD; G. Sopko, MD; and M. Terrin, MD; Mortality and morbidity classification committee: M. Weisfeldt, MD (chairman); W. Baker, MD; M. Cowley, MD; K. Kent, MD; E. Luchstein, MD; T. Robertson, MD; L. Scherlis, MD; and M. Terrin, MD; Safety and data monitoring committee: F. Klocke, MD (chairman); J. Bailar, MD; R. Conti, MD; D. DeMets, PhD; V. Fuster, MD; T. Killip, MD; H. Roberts, MD; L. Walters, PhD; Ex-officio members: E. Braunwald, MD; G. Knatterud, PhD; E. Passamani, MD; and T. Robertson, MD; Steering committee: members of the steering committee are the study chairman and the principal investigators from the TIMI clinical centers, core laboratories, coordinating center, and National Heart, Lung, and Blood Institute program office.

References

KEY WORDS • acute myocardial infarction • thrombolysis • rt-PA • coronary angioplasty • coronary artery disease • cardiac catheterization
One-year results of the Thrombolysis in Myocardial Infarction investigation (TIMI) 
Phase II Trial.
D O Williams, E Braunwald, G Knatterud, J Babb, J Bresnahan, M A Greenberg, A Raizner, A Wasserman, T Robertson and R Ross

_Circulation_. 1992;85:533-542
doi: 10.1161/01.CIR.85.2.533

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/85/2/533

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/