Antibiotic Therapy After Acute Myocardial Infarction
A Prospective Randomized Study

Ralf Zahn, MD, FESC; Steffen Schneider, PhD; Birgit Frilling, MD; Karlheinz Seidl, MD, FESC; Ulrich Tebbe, MD, FESC; Michael Weber, MD; Martin Gottwik, MD, FESC; Ernst Altmann, MD; Friedrich Seidel, MD; Jürgen Rox, MD; Ulrich Höffler, MD; Karl-Ludwig Neuhaus, MD, FESC; Jochen Senges, MD, FESC; for the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte (Working Group of Leading Hospital Cardiologists; ALKK)

Background—Infection with \textit{Chlamydia pneumoniae} is suspected to contribute to the pathogenesis of human atherosclerosis. We investigated whether treatment with the macrolide antibiotic roxithromycin would reduce mortality or morbidity in patients with an acute myocardial infarction.

Methods and Results—Eight hundred seventy-two patients with an acute myocardial infarction (AMI) were randomly assigned to receive double-blind treatment with either 300 mg roxithromycin or placebo daily for 6 weeks. Primary end point was total mortality during 12-month follow-up. Four hundred thirty-three patients were treated with roxithromycin and 439 with placebo. With the exception of a higher proportion of patients suffering an anterior wall AMI (48.1% in the roxithromycin group versus 40.2% in the placebo group; \textit{P}=0.027) and a lower prevalence of chronic obstructive pulmonary disease in the roxithromycin group (3.5% versus 6.9%, \textit{P}=0.028), baseline characteristics, reperfusion therapy, and medical treatment were well balanced between the two groups. More patients in the roxithromycin group interrupted their study medication before completion of at least 4 weeks of treatment (78 of 433 [18%] versus 48 of 439 [11%]; \textit{P}=0.003; odds ratio, 1.8; 95% CI, 1.2 to 2.6). Follow-up at 12 months was achieved in 868 of 872 (99.5%) patients. Total mortality at 12 months was 6.5% (28 of 431) in the roxithromycin group compared with 6.0% (26 of 437) in the placebo group (odds ratio, 1.1; 95% CI, 0.6 to 1.9; \textit{P}=0.739). There were also no differences in the secondary combined end points at 12 months.

Conclusions—Treatment of AMI patients with roxithromycin did not reduce event rates during 12 months of follow-up. Therefore, our findings do not support the routine use of antibiotic treatment with a macrolide in patients with AMI. (Circulation. 2003;107:1253-1259.)

Key Words: myocardial infarction ■ mortality ■ morbidity ■ infection

Inflammation plays a crucial role in the pathogenesis of arteriosclerosis, especially in acute coronary syndromes. Seroepidemiological studies have raised the question of whether bacterial infections, especially with \textit{Chlamydia pneumoniae}, may contribute to this inflammatory process.\textsuperscript{1,2} Histopathologic studies show a higher prevalence of \textit{Chlamydia pneumoniae} in diseased versus normal coronary arteries.\textsuperscript{3,4} Animal models also seem to support an active role of this agent in the pathogenesis of arteriosclerosis.\textsuperscript{5,6} Therefore, therapy with a macroide antibiotic may favorably influence the natural course in patients with coronary heart disease. Several small clinical studies in patients with acute coronary syndromes showed a potential beneficial effect of such a treatment.\textsuperscript{7-10} However, no definitive conclusions could be drawn, and a more recent study found no effect of such a therapy on clinical events.\textsuperscript{11,12} The purpose of the present study (Antibiotic Therapy After an Acute Myocardial Infarction [ANTIBIO]) was to determine the influence of treatment with the macrolide antibiotic roxithromycin in patients with acute myocardial infarction (AMI).

See p 1228

Methods

The ANTIBIO study was a prospective, randomized, placebo-controlled, double-blind study to investigate the effect of treatment...
with roxithromycin in patients with AMI. The ethics committees of the participating hospitals approved the study.

Patients and Hospitals

Patients presenting with an ST-elevation or non–ST-elevation AMI within 48 hours after symptom onset were randomized within 5 days after admission to either a 6-week treatment with the macrolide antibiotic roxithromycin 300 mg daily or placebo.

AMI was diagnosed in the presence of the following 3 criteria: (1) persistent angina pectoris lasting >20 minutes; (2) elevation of creatinine kinase >3 times the normal upper limit with significant CK-MB fraction or elevation of troponin T or troponin I; and (3) changes in ECG consistent with either ST-elevation myocardial infarction (ST segment elevation of ≥1 mm in at least 2 standard leads or ≥2 mm in at least 2 contiguous precordial leads or the presence of a left bundle branch block) or ST segment depression of >1 mm in 2 contiguous leads or inversion of the T waves of >1 mm in at least 3 contiguous leads (non–ST-elevation myocardial infarction).

Exclusion criteria were participation in another study, pregnancy, lactation, allergy to roxithromycin or other macrolides, clinically relevant diseases of the liver or the central nervous system or other systemic diseases that could interfere with adherence to the study protocol, concomitant use of ergotamine- or dihydroergotamine-containing drugs, and foreseeable inability to complete the follow-up.

Inclusion of patients did not depend on results of serological tests for previous infection with *Chlamydia pneumoniae*. Such tests were also not suggested by the study protocol. Patients were eligible for the intention-to-treat analysis if they were randomized.

The study was performed mainly by hospitals cooperating with the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte (ALKK) and some other hospitals. The participating hospitals represented large community centers as well as tertiary care centers.

Randomization, Treatment, and Follow-Up

Randomization was separately performed at each participating center using coded envelopes provided by the Heart Center Ludwigshafen. A block-wise randomization for each center with blocks of 8 patients was used. The randomization codes were sealed in closed envelopes, which were opened only if considered necessary for the treatment of severe adverse events. Each randomized patient had to be immediately reported via fax to the data collection center at the Heart Center Ludwigshafen (S. Schneider, PhD). The total test level was therefore determined via the restricted procedure method reported by Whitehead.15 The proposed decision to stop the study was based on 1% significance level for differences in total 8-week mortality, and the tests were performed by the independent Institute of Biometrics at the Heart Center Ludwigshafen (S. Schneider, PhD). The total test level was therefore adjusted according to Bonferroni’s method to a 2-sided α-level of 4%, with an 80% power to detect a significant difference. This resulted in a calculated total sample size of 3922 patients. After continuous slow recruitment of patients, the steering committee decided to extend the initial recruitment period. Because recruitment did not improve substantially, the study was stopped in March 2001 after inclusion of 872 patients.

The patients gave written informed consent for participating in the study and processing of their anonymous data. All data sheets were sent to the central data processing center (Institute of Biometrics, Heart Center Ludwigshafen).

Absolute numbers, percentages, and medians were computed to describe the patient population. Categorical values were compared by χ² analysis or Fisher’s exact test as appropriate. Continuous variables were compared by Wilcoxon rank-sum test.

Kaplan-Meier curve was produced to describe survival, and the difference between groups was analyzed with the log-rank test.

Primarily, all analyses were done on an intention-to-treat basis. In addition, multiple logistic regression analysis was used to control for differences in baseline characteristics (anterior wall AMI or chronic obstructive pulmonary disease) between the 2 treatments groups concerning the primary and secondary end points. Furthermore, end points were analyzed according to treatment per protocol, that is, at least 4 of 6 weeks of treatment. All probability values are results of 2-tailed tests. The tests were performed using the SAS statistical package, version 6.12.

Role of the Funding Source

Aventis Pharma gGmbH, Germany, supported the trial financially without taking influence on the design of the trial, collection, analysis, and interpretation of the data.

Results

Inclusion of patients started on September 1999. End of inclusion was planned for December 2000 and extended to April 2001. Sixty-eight hospitals all over Germany participated. Eight hundred seventy-two patients were included, 433 treated with roxithromycin and 439 with placebo (Figure 1). Treatment was started at a median of 4 days (quartiles: 2/6 days) after the onset of symptoms.

ST-elevation myocardial infarction occurred in 88% of patients. With the exception of a higher proportion of patients with an ST-elevation myocardial infarction suffering an anterior wall AMI (48.1% in the roxithromycin group versus new elevation of >50% of the last measured value in the case of still-persistent elevated values. Postinfarction angina was defined as any angina pectoris within 2 weeks after the index AMI. Stroke was defined as development of a new neurological deficit persisting >24 hours. Cerebral imaging was not mandatory.

Two physicians (B.F. and R.Z.) examined all patient files to determine whether the events recorded fulfilled criteria of either primary or secondary end points. This was done before the treatment code was opened.

Statistical Analysis

Presumed clinical event rates were estimated according to previous data from ALKK studies on AMI, the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) registry13,14 and the Myocardial Infarction Registry (MIR).13,14 A total mortality rate after 12 months of 10% in the placebo group and a 30%-lower mortality rate in the active treatment group (7% mortality) were assumed. For safety reasons, total mortality at 8 weeks after randomization was monitored in a sequential design (triangular test) according to the restricted procedure method reported by Whitehead.15 The proposed decision to stop the study was based on 1% significance level for differences in total 8-week mortality, and the tests were performed by the independent Institute of Biometrics at the Heart Center Ludwigshafen (S. Schneider, PhD). The total test level was therefore adjusted according to Bonferroni’s method to a 2-sided α-level of 4%, with an 80% power to detect a significant difference. This resulted in a calculated total sample size of 3922 patients. After continuous slow recruitment of patients, the steering committee decided to extend the initial recruitment period. Because recruitment did not improve substantially, the study was stopped in March 2001 after inclusion of 872 patients.

The patients gave written informed consent for participating in the study and processing of their anonymous data. All data sheets were sent to the central data processing center (Institute of Biometrics, Heart Center Ludwigshafen).

Absolute numbers, percentages, and medians were computed to describe the patient population. Categorical values were compared by χ² analysis or Fisher’s exact test as appropriate. Continuous variables were compared by Wilcoxon rank-sum test.

Kaplan-Meier curve was produced to describe survival, and the difference between groups was analyzed with the log-rank test.

Primarily, all analyses were done on an intention-to-treat basis. In addition, multiple logistic regression analysis was used to control for differences in baseline characteristics (anterior wall AMI or chronic obstructive pulmonary disease) between the 2 treatments groups concerning the primary and secondary end points. Furthermore, end points were analyzed according to treatment per protocol, that is, at least 4 of 6 weeks of treatment. All probability values are results of 2-tailed tests. The tests were performed using the SAS statistical package, version 6.12.
40.2% in the placebo group, \( P = 0.027 \) and a lower prevalence of chronic obstructive pulmonary disease in the roxithromycin group (3.5% versus 6.9%, \( P = 0.028 \), baseline characteristics were well balanced between the two groups (Table 1). No differences between the two treatment groups were observed regarding the type of AMI, use of reperfusion therapy, and acute as well as discharge medical therapy (Table 2).

Treatment with roxithromycin was significantly more often undertaken for \(< 4\) weeks instead of the planned 6 weeks compared with treatment with placebo (78 of 433 [18%] versus 48 of 439 [11%]; \( P = 0.003 \); odds ratio [OR], 1.8; 95% CI, 1.2 to 2.6) (Figure 1).

There were no significant differences in the event rates until hospital discharge (Table 3). Follow-up at 12 months could be achieved in 868 of 872 (99.5%) patients (99.5% in the roxithromycin group versus 99.5% in the placebo group). Total mortality at 12 months was 6.5% (28 of 431) in the roxithromycin group compared with 6.0% (26 of 437) in the placebo group (OR, 1.1; 95% CI, 0.6 to 1.9, \( P = 0.739 \)) (Figure 2). There were also no differences at 12 months for the combined end points (Table 3). After adjusting for differences in baseline characteristics, 12-month mortality was still not significantly different between the 2 groups (multivariate OR, 1.1; 95% CI, 0.6 to 2.0; \( P = 0.797 \)). There were also no significant differences in the secondary end

**TABLE 1. Baseline Characteristics and Concomitant Diseases**

<table>
<thead>
<tr>
<th></th>
<th>Roxithromycin, n=433 (100%)</th>
<th>Placebo, n=439 (100%)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y*</td>
<td>60.4 (51.3 to 69.1)</td>
<td>61.0 (52.2 to 68.6)</td>
<td>0.689</td>
</tr>
<tr>
<td>Male sex</td>
<td>342 of 433 (79.0%)</td>
<td>349 of 439 (79.5%)</td>
<td>0.851</td>
</tr>
<tr>
<td>STEMI</td>
<td>377 of 433 (87.1%)</td>
<td>390 of 439 (88.8%)</td>
<td>0.422</td>
</tr>
<tr>
<td>Anterior wall infarction (in case of STEMI)</td>
<td>181 of 376 (48.1%)</td>
<td>156 of 388 (40.2%)</td>
<td>0.027</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>13 of 433 (3.0%)</td>
<td>17 of 436 (3.9%)</td>
<td>0.469</td>
</tr>
<tr>
<td>Heart failure at admission</td>
<td>37 of 433 (8.6%)</td>
<td>37 of 437 (8.5%)</td>
<td>0.967</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>17 of 433 (3.9%)</td>
<td>16 of 439 (3.6%)</td>
<td>0.828</td>
</tr>
<tr>
<td>Left bundle-brunch block</td>
<td>5 of 432 (1.2%)</td>
<td>8 of 439 (1.8%)</td>
<td>0.418</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>25 of 432 (5.8%)</td>
<td>19 of 438 (4.3%)</td>
<td>0.329</td>
</tr>
<tr>
<td>Days from symptom onset to randomization*</td>
<td>4.0 (2.0 to 5.0)</td>
<td>4.0 (2.0 to 6.0)</td>
<td>0.221</td>
</tr>
<tr>
<td>Concomitant diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>22 of 427 (5.2%)</td>
<td>17 of 432 (3.9%)</td>
<td>0.392</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>15 of 424 (3.5%)</td>
<td>29 of 421 (6.9%)</td>
<td>0.028</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>210 of 423 (49.7%)</td>
<td>229 of 428 (53.5%)</td>
<td>0.260</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>68 of 429 (15.9%)</td>
<td>71 of 432 (16.4%)</td>
<td>0.816</td>
</tr>
<tr>
<td>Present smoker</td>
<td>213 of 425 (50.1%)</td>
<td>215 of 426 (50.5%)</td>
<td>0.918</td>
</tr>
</tbody>
</table>

STEMI indicates ST-elevation myocardial infarction.

*Median and quartiles.
patients with coronary heart disease could perhaps profit from triggering factor for progression of arteriosclerosis. 1,2 *Chlamydia pneumoniae* was identified to be a potential causative or exaggerating the progress of arteriosclerosis. It maintains an inflammatory process in the vessel wall, thus or chronic viral or bacterial infections may trigger and/or be important in the pathogenesis of arteriosclerosis. Recurrent analyses also showed no differences at 12 months for the intended 6 weeks, 12-month mortality was 7.1% (25 of 353) in the roxithromycin group and 6.2% (24 of 390) in the placebo group (OR, 1.2; 95% CI, 0.7 to 2.1; \( P = 0.353 \)). If only those patients were analyzed who had been undergoing treatment with the study medication for at least 4 points. If only those patients were analyzed who had been undergoing treatment with the study medication for at least 4 of the intended 6 weeks, 12-month mortality was 7.1% (25 of 353) in the roxithromycin group and 6.2% (24 of 390) in the placebo group (OR, 1.2; 95% CI, 0.7 to 2.1; \( P = 0.611 \)). These analyses also showed no differences at 12 months for the combined end points.

## Discussion

Traditional risk factors, eg, sex, hyperlipidemia, cigarette smoking, diabetes mellitus, family history of cardiovascular disease, and arterial hypertension, are often prevalent in patients with cardiovascular disease, but they predict < 50% of all future cardiovascular events.16 Inflammation plays a crucial role in the pathogenesis of arteriosclerosis. Recurrent or chronic viral or bacterial infections may trigger and maintain an inflammatory process in the vessel wall, thus exaggerating the progression of arteriosclerosis. *Chlamydia pneumoniae* was identified to be a potential causative or triggering factor for progression of arteriosclerosis.1,2 Macrolides are the antibiotic of choice to treat infections with *Chlamydia pneumoniae*. Another possible action of macrolides could be their anti-inflammatory effects.17 Therefore, patients with coronary heart disease could perhaps profit from adding an antibiotic to standard medical treatment.

### Characteristics of Patients and Acute Treatment

Eight hundred seventy-two patients from 68 centers were eligible to be included in the ANTIBIO study. ST-elevation myocardial infarction was present in 88% of patients. Mean age was 61 years, which is much lower than the mean age of 67 years in the MITRA and MIR registries.13,14 Because there was no age limit for inclusion of patients, the observed low mean age indicates a selection of patients, perhaps an effect of performing a randomized study instead of a registry. This selection, together with the high rate (75%) of reperfusion therapy in ST-elevation myocardial infarction patients and high rates of concomitant therapy with \( \beta \)-blockers, ACE inhibitors, and statins, may explain the low in-hospital death rate of < 2% as well as the lower than expected death rate at 12 months. On the basis of data from the MITRA studies,13,18 we assumed a 1-year mortality of 10%. However, we found a 6% death rate in the placebo group.

Discontinuation of the study drug was higher for roxithromycin (18%) than for placebo (11%; \( P = 0.003 \)). However, there were no significant differences in any specific reason for the discontinuation. A higher overall noncompliance rate in the roxithromycin group was expected and has been previously shown in other trials.

### Treatment Effects

Small studies in patients with acute coronary syndromes that either tried to reduce the frequency of viral infections19 or used macrolide antibiotics to treat suspected chronic chlamydial infections8–9 showed promising results. The Roxithromycin Ischemic Pilot Study (ROXIS) examined the effect of a 30-day treatment with roxithromycin in 202 patients with unstable angina or non–Q-wave myocardial infarction. At 31 days, clinical outcome was better in the roxithromycin group.7 This effect was maintained during follow-up; however, it was no longer significant.8 Gupta et al10 analyzed the effect of treatment with azithromycin at up to 6 days in 213 patients with stable coronary artery disease. In patients seropositive for antibodies against *Chlamydia pneumoniae*, event rates after 18 months were reduced. The Clarithromycin

### Table 2. Acute Reperfusion Therapy and Concomitant Medication During the First 48 Hours After Admission and at Discharge

<table>
<thead>
<tr>
<th>Medication at discharge</th>
<th>Roxithromycin</th>
<th>Placebo</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>n=425 (100%)</td>
<td>n=410 (100%)</td>
<td>...</td>
</tr>
<tr>
<td>Clopidogrel or ticlopidine</td>
<td>213 of 424 (50.2%)</td>
<td>219 of 431 (50.8%)</td>
<td>0.866</td>
</tr>
<tr>
<td>Statins</td>
<td>321 of 425 (75.5%)</td>
<td>313 of 431 (72.6%)</td>
<td>0.332</td>
</tr>
<tr>
<td>( \beta )-Blockers</td>
<td>391 of 424 (90.3%)</td>
<td>384 of 431 (87.5%)</td>
<td>0.322</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>344 of 425 (80.9%)</td>
<td>344 of 431 (79.8%)</td>
<td>0.678</td>
</tr>
<tr>
<td>Other antibiotic than macrolide</td>
<td>16 of 424 (3.8%)</td>
<td>17 of 430 (4%)</td>
<td>0.892</td>
</tr>
</tbody>
</table>

STEMI indicates ST-elevation myocardial infarction.
in Acute Coronary Syndrome Patients in Finland (CLARIFY) study also showed a beneficial effect of a 3-month therapy with clarithromycin in 148 patients with acute non-Q-wave coronary syndromes after 1.5 years.\textsuperscript{10} The recently presented results of the South Thames trial of antibiotics in myocardial infarction and unstable angina (STAMINA) trial also showed a superiority of a combination antibiotic therapy after 1 year in 324 patients with acute coronary syndromes.\textsuperscript{20} In contrast to these studies, we found no beneficial effect of a 6-week treatment with roxithromycin 300 mg daily in 872 patients with AMI during a follow-up of 12 months. There was no difference in total mortality (6.5\% in the roxithromycin group compared with 6.0\% in the placebo group; OR, 1.1; 95\% CI, 0.6 to 1.9, \(P=0.739\)) and no differences at 12 months for the combined end point of death, myocardial infarction, stroke, or angina pectoris leading to hospitalization (25.1\% versus 20.8\%, \(P=0.138\)). These results remained unchanged when we adjusted for differences in patients’ characteristics between the 2 groups or analyzed only the data of patients on treatment per protocol.

Our findings are supported by the Azithromycin in Coronary Artery Disease: Elimination of Myocardial Infection with Chlamydia (ACADEMIC) study.\textsuperscript{11} In 302 patients seropositive for Chlamydia pneumoniae with stable coronary artery disease, no beneficial effect of a 3-month treatment with azithromycin was found after 6 months. At the 51st Annual Scientific Session of the American College of Cardiology in 2002, results of two other large randomized controlled clinical trials on macrolide treatment in patients with coronary artery disease were presented: the Azithromycin in Acute Coronary Syndrome (AZACS) study of a 5-day azithromycin treatment in 1412 patients with acute coronary syndromes and the Weekly Intervention with Azithromycin for Atherosclerosis and its related Disorders (WIZARD) study of a 3-month treatment with azithromycin in 3868 patients stable after an AMI who were seropositive for Chlamydia pneumoniae. Both studies showed no clinical benefit of macrolide treatment during follow-up.

In summary, all these data show conflicting results for the value of an antibiotic therapy in patients with coronary artery disease.
Conclusions

Antibiotic therapy with roxithromycin for 6 weeks in patients with an AMI did not result in better clinical outcome during 1 year of follow-up. This finding challenges the hypothesis of a major role of Chlamydia pneumoniae in the pathogenesis of arteriosclerosis.

Limitations of the Study

The premature termination of our study after 872 patients, 22.2% of the initially calculated sample size of 3922 patients, might have influenced our ability to detect a significant difference between the 2 groups. However, if we estimated the chance to detect such a difference for the initially planned sample size using our actual data of the 872 patients, we found that we would have not been able to demonstrate a significant difference between the 2 groups. This may be attributable in part to the lower than expected incidence of end points. We included patients without measurement of their serum antibody titers for Chlamydia pneumoniae. A study by Neumann et al21 found a reduction in neointima proliferation with roxithromycin treatment after coronary stent implantation only in patients with high antibody titers. From our data, we cannot exclude that such a subgroup of patients might benefit from roxithromycin treatment.

Appendix

Members of the ANTIBIO Study Group
Principal Investigator: R. Zahn

Members of the Steering Committee
J. Senges (chairman), U. Tebbe, M. Weber, K.L. Neuhaus (Dr Neuhaus died before the end of the study)

Members of the Data and Safety Monitoring Board
R. Schröder (chairman), W. Stille, H. Katus, R. Dietz; Statistical Analysis: S. Schneider, K.E. Siegler; Advisory Board: U. Höfler, M. Gottwik

Critical Events Committee
B. Frilling, R. Zahn; Study coordination: H. Dehn

Participating centers and Number of Included Patients

Städtisches Klinikum, Ludwigshafen (86), Städtisches Klinikum, Dresden (35), Städt. Klinikum, Dessau (35), Städtisches Klinikum, Kempten (34), Allgemeines Krankenhaus, Hagen (32), Johanniter Krankenhaus, Geesthacht (31), Städtisches Klinikum, Nürnberg (30), Marien Hospital, Wesel (27), Evangelisches Krankenhaus, Oberhausen (24), Evangelisches Krankenhaus, Unna (20), Marienkrankenhaus, Soest (19), Evangelisches Krankenhaus, Düsseldorf (19), Augusta-Krankenanstalt, Bochum (19), Kreisklinik, Dachau (18), EKA Erzgebirgsklinikum, Annaberg-Buchholz (18), St. Anna Hospital, Heme (17), Kreiskrankenhaus, Eschwege (17), Theresien-Krankenhaus, Mannheim (16), Städtisches Klinikum, Rosenheim (16), Krankenhaus Moabit, Berlin (16), Kreiskrankenhaus, Demmin (16), Städtisches Krankenhaus, Siegburg (16), Klinikum Lippe, Detmold (16), Kreiskrankenhaus, Blankenburg (14), Herzcenter Kaiser-Wilhelm Krankenhaus, Duisburg (14), St Marien-Hospital, Lünen (14), Klinikum Ludwigsburg-Bietigheim, Ludwigsburg (13), Aachenbacher Krankenhaus, Königs-Wusterhausen (13), Kreiskrankenhaus, Leer (13), Städtisches Klinikum, Göttingen (12), Kreiskrankenhaus, Schleiz (12), Städtische Kliniken, Oldenburg (11), Knappschafts-Krankenhaus, Recklinghausen (11), Ruppiner Kliniken, Neuruppin (10), Augusta-Krankenhaus, Düsseldorf (10), Evangelisches Stift St. Martin, Koblenz (10) Städtisches Krankenhaus Holweide, Köln (10), St. Franziskus Hospital, Münster (9), Kreiskrankenhaus, Aschersleben (9), Evangelisches Krankenhaus, Mülheim (8), Städt. Krankenhaus Siloah, Hannover (6), Städtisches Klinikum, Krefeld (6), Städtische Kliniken, Offenbach (6), Kreiskrankenhaus Bürgerhospital, Friedberg (6), Berufsgenossenschaftliche Kliniken Bergmannstrost, Halle (6), Städtisches Krankenhaus, Wolfenbüttel (6), Kreiskrankenhaus, Altötting (5), Johanniter Krankenhaus, Duisburg (5), Kreiskrankenhaus, Gifhorn (5), DRK Krankenhaus Westerwald, Hachenburg (5), Kreiskrankenhaus, Neustadt a.d. Aisch (4), St. Marienhospital, Gelsenkirchen-Bür (4), Kreiskrankenhaus, Rudolstadt (4), Städt. Krankenhaus, Lüneburg (4), Kreiskrankenhaus, Mechernich (4), Kreiskrankenhaus Land Hadeln, Otterdorfer Kreiskrankenhaus, Waldbröl (3), Kreiskrankenhaus, St. Ingbert (3), Städt. Klinikum, Pforzheim (3), Diakonissenkrankenhaus, Dresden (3), Klinikum Coburg (2), Städtisches Klinikum, Quedlinburg (2), Ev. Krankenhaus Bad Godesberg, Bonn (2), Robert-Bosch-Krankenhaus, Stuttgart (1), Zentralkrankenhaus Reinkenheim, Bremerhaven (1), Klinikum der Landeshauptstadt, Wiesbaden (1), Kreiskrankenhaus, Rorschütz (1), Marienhospital, Bottrop (1).


Antibiotic Therapy After Acute Myocardial Infarction: A Prospective Randomized Study
for the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte (Working Group of Leading Hospital Cardiologists; ALKK)

Circulation. 2003;107:1253-1259; originally published online February 17, 2003;
doi: 10.1161/01.CIR.0000054613.57105.06
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 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/107/9/1253

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/