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Comparing Lansoprazole and Omeprazole in Onset of Heartburn Relief: Results of a Randomized, Controlled Trial in Erosive Esophagitis Patients

Joel E. Richter, M.D., Peter J. Kahrilas, M.D., Stephen J. Sontag, M.D., Thomas O. G. Kovacs, M.D., Bidan Huang, Ph.D., and Jennifer L. Pencyla, B.S.

The Cleveland Clinic Foundation, Cleveland, Ohio; Northwestern University Medical School, Chicago, Illinois; Veterans Affairs Hospital, Hines, Illinois; University of California Los Angeles Medical Center/Center for Ulcer Research and Education Clinic, Los Angeles, California; Abbott Laboratories, Abbott Park, Illinois; and TAP Pharmaceutical Products, Lake Forest, Illinois

OBJECTIVE: This randomized, double-blind, multicenter study was conducted to confirm a previous finding that lansoprazole relieves heartburn faster than omeprazole in patients with erosive esophagitis.

METHODS: A total of 3510 patients with erosive esophagitis and at least one episode of moderate to very severe daytime and/or nighttime heartburn during the 3 days immediately before the screening visit were randomized to lansoprazole 30 mg once daily or omeprazole 20 mg once daily for 8 wk. Patients recorded the presence and severity of daytime and nighttime heartburn in daily diaries. On treatment days 1–4, patients were telephoned to confirm the completion of their daily diary. The primary efficacy parameters were the percentage of heartburn-free days and heartburn-free nights, as well as the average severity of daytime and nighttime heartburn.

RESULTS: During treatment day 1 and all evaluation time points including the entire 8-wk treatment period, significantly ($p < 0.05$) higher percentages of patients treated with lansoprazole than those treated with omeprazole did not experience a single episode of heartburn. Onset of heartburn relief was more rapid in lansoprazole-treated *versus* omeprazole-treated patients: on day 1, 33% *versus* 25% of lansoprazole- *versus* omeprazole-treated patients were heartburn-free. The percentages of heartburn-free days and heartburn-free nights were also significantly ($p < 0.01$) greater for patients treated with lansoprazole at all evaluation time points. Heartburn severity was significantly less among those treated with lansoprazole compared with omeprazole. Both treatments were safe and well tolerated.

CONCLUSIONS: Over 8 wk, lansoprazole 30 mg once daily relieved heartburn symptoms faster and more effectively than omeprazole 20 mg once daily in patients with erosive esophagitis. (Am J Gastroenterol 2001;96:3089–3098. © 2001 by Am. Coll. of Gastroenterology)

INTRODUCTION

Heartburn, the hallmark symptom of gastroesophageal reflux disease (GERD), affects an estimated 25 million individuals on a daily basis and 60 million on a monthly basis in the United States (1). Results of North American studies suggest that between 40% and 60% of those with GERD have esophagitis (2–4). Regardless of whether esophagitis is present, GERD symptoms negatively affect patients' daily lives. Those with GERD generally report decreases in productivity, quality of life, and overall well-being (5, 6). One study found that patients with GERD rated their quality of life lower than those with untreated angina pectoris or heart failure (7).

In addition to its negative impact on patients' quality-of-life, GERD may increase the risk of serious sequelae. Significant increases in the incidences of adenocarcinomas of the esophagus and gastric cardia (8–10) have occurred over the past several years, and a recent study showed a causal relationship between GERD and esophageal adenocarcinoma (11). In a large Swedish study, those who reported heartburn, regurgitation, or both at least once weekly had an 8-fold greater risk of developing esophageal cancer than those with no symptoms (11). Patients reporting nighttime symptoms of GERD had an even higher (11-fold) risk.

In patients with GERD, the goals of treatment are prompt and effective relief of symptoms, healing of esophagitis (if present), and reduction in the risk for complications. Numerous studies have confirmed that the proton pump inhibitors are superior to the histamine-2 receptor antagonists in relieving reflux symptoms, healing esophagitis, and preventing relapse of esophagitis (12–17). A large multicenter study of patients with erosive reflux esophagitis found that lansoprazole 30 mg once daily and omeprazole 20 mg once daily produced comparable rates of mucosal healing (18). However, in this study as well as in a meta-analysis by Huang and colleagues (19), significantly higher percentages of patients treated with lansoprazole 30 mg reported relief of their

Table 1. Esophagitis Grading Scale

Grade	Description
0	Mucosa normal in appearance
1	Mucosal edema, hyperemia, and/or friability of mucosa
2	One or more erosions/ulcerations involving <10% of distal 5 cm of the esophagus
3	Erosions/ulcerations involving 10–50% of distal 5 cm of esophagus, or an ulcer measuring 3–5 mm in diameter
4	Multiple erosions/ulcerations involving >50% of distal 5 cm of esophagus, or a single large ulcer >5 mm in diameter

heartburn symptoms compared to patients treated with omeprazole 20 mg (18, 19).

Although many studies have compared the proportions of patients who report relief of reflux symptoms after a ≥1-wk course of treatment, few have carefully evaluated the rapidity of heartburn resolution. The purpose of this study was to compare the onset and effectiveness of heartburn relief in patients with endoscopically-confirmed erosive esophagitis treated with lansoprazole or omeprazole.

MATERIALS AND METHODS

Study Design and Patient Selection

The study was conducted as a Phase III, double-blind, parallel-group, multicenter clinical trial. The institutional review board of each participating study site approved the study protocol before study initiation. All patients provided written informed consent before initiation of any study-related procedures.

Patients who were ≥18 yr of age with endoscopically-confirmed erosive esophagitis of grade 2 or higher were eligible for study enrollment. The esophagitis grading scale is described in Table 1. Patients were required to have had at least one episode of moderate to very severe daytime and/or nighttime heartburn during the 3 days immediately before the screening visit (assessed by a retrospective heartburn questionnaire). Patients were excluded from study participation if they had active duodenal or gastric ulcers of ≥3 mm in diameter; coexisting systemic disease affecting the esophagus (*e.g.*, scleroderma); esophageal stricture requiring dilation; a history of GI bleeding or gastric, duodenal, or esophageal surgery; clinically significant abnormal laboratory values or disease; chronic use of ulcerogenic drugs, including nonsteroidal anti-inflammatory drugs or systemic corticosteroids or >325 mg/day of aspirin; or evidence of current alcohol or drug abuse. Patients receiving proton pump inhibitor or histamine-2 receptor antagonist therapy discontinued use of the antisecretory agent 2 wk or within 1 day, respectively, of study initiation. Women who were pregnant or lactating were excluded from study participation.

Patients meeting the study entry criteria were randomized in a 1:1 ratio to receive either lansoprazole 30 mg or omeprazole 20 mg once daily for 8 wk. Both study medications were overencapsulated in gray opaque capsules to maintain the study blind for the patients, investigators, study personnel, and sponsor. Patients were instructed to take the study medication each morning before breakfast. They were dispensed a daily diary and were asked to return for study visits at the conclusion of 1, 2, and 8 wk of treatment.

Study Procedures

Complete medical history, physical examination, and laboratory assessments (including hematology, chemistry, urinalysis, serology for *Helicobacter pylori*, and pregnancy testing in female patients) were performed during screening. Medical evaluation including vital sign monitoring, review of concurrent medications, and assessment of adverse events were performed at the wk 1, 2, and wk 8 or final follow-up visits.

Patients recorded the presence and severity of daytime and nighttime heartburn in their daily diaries. The severity of symptoms was recorded as follows: none; mild (occasional, could be ignored, does not influence daily routine or sleep); moderate (heartburn cannot be ignored and/or occasionally influences daily routine or sleep); severe (heartburn present most of the day or night and regularly influences daily routine or sleep); or very severe (constant heartburn and/or heartburn that markedly influences daily routine or sleep). All patients were contacted by telephone during days 1–4 of treatment to confirm that the daily diary was being completed and that the study drug was being taken. During the telephone survey, patients reported the severity of daytime and nighttime heartburn using the same grading scale as in the patient diary. These diaries were completed retrospectively (*e.g.*, on day 2 subjects entered diary data for day 1).

The safety of the treatment was determined by systematic assessments of adverse events. Patients were instructed to return all drug supplies at the end of treatment wk 1, 2, and 8. All remaining capsules were counted as a method for assessing compliance with the prescribed regimen.

Statistical Analysis

A sample size of 3500 patients was planned so that the study had a 95% power to detect differences between lansoprazole and omeprazole at the 0.0025 (two-tailed) level, assuming that the mean and SD for the percentage of days with heartburn over days 1–3 of treatment would be 42.7% (40.0%) for subjects treated with lansoprazole and 49.3% (41.3%) for subjects treated with omeprazole. A p value of 0.0025 was chosen to demonstrate that the strength of the efficacy results would be equivalent to that of efficacy results obtained in two independent studies using a p value of 0.05.

Data were analyzed using the intent-to-treat approach, which included all patients who entered the study with endoscopically confirmed erosive esophagitis, received at least one dose of study drug, and completed diaries regardless of any protocol deviation. Similar analyses were per-

formed using the evaluable patient population (*i.e.*, those patients who complied with the protocol).

The efficacy variables included the frequency and severity of daytime and nighttime heartburn experienced by patients on day 1 of treatment and during days 1–3 (primary), wk 1, wk 1 and 2, and the entire 8 wk of treatment. The available patient daily diary entries reflecting the evaluated time period were used.

The percentages of heartburn-free days, heartburn-free nights, and patients who did not have a single episode of heartburn were compared between the treatment groups using the Cochran-Mantel-Haenszel test, with the investigative site as stratum. Heartburn symptom severity of none, mild, moderate, severe, and very severe was scored as 0, 1, 2, 3, and 4, respectively. The average heartburn severity over the time period was calculated for each patient, and treatment group comparisons were performed using the van Elteren method of combining the Wilcoxon test statistics, with investigative site as stratum (20). Because of the large size of the study population, the mean and SD of the average heartburn severity is presented for each treatment group. Stratification of outcomes with baseline heartburn severity, baseline demographic characteristics (sex, age [$<$40 yr, 40–59 yr, or $\geq$60 yr], ethnicity, and alcohol, tobacco, and caffeine consumption), and baseline esophagitis grade (grade 2, 3, or 4) also was performed using the van Elteren method. Sustained resolution of heartburn was defined as 7 consecutive days with no heartburn. The cumulative proportions of patients who reached the start of sustained resolution by days 1, 3, 7, 14, 28, and 56 were calculated and the time to sustained resolution compared between treatment groups using the log-rank test. The percentages of heartburn-free days and of heartburn-free nights using phone records reflecting days 1–3 of treatment were analyzed, similar to the patient diary findings.

Comparison between the treatment groups for treatment-emergent adverse events was performed using the Fisher's exact test. The mean number of days to onset of diarrhea was compared between the treatment groups using the analysis of variance, with treatment as the factor.

RESULTS

Patient Characteristics

A total of 3510 patients from 162 sites were randomized to the two treatment groups: 1754 to lansoprazole 30 mg, and 1756 to omeprazole 20 mg. No significant differences in demographic parameters were noted between the treatment groups, with one exception. A significantly higher percentage of patients randomized to omeprazole as compared to lansoprazole reported tobacco use (28% *vs* 25%, $p \leq 0.05$) (Table 2). Similar percentages of patients in both groups were *H. pylori* positive, and the majority of patients in both groups were considered to have grade 2 esophagitis.

Analyses of the retrospective heartburn questionnaire revealed that, at baseline, the treatment groups were similar with respect to percentages of days with heartburn, average severity of daytime heartburn, and average severity of nighttime heartburn. A statistically significantly higher percentage of nights with heartburn was observed among those randomized to lansoprazole as compared to those randomized to omeprazole at baseline (84% *vs* 82%, $p \leq 0.05$).

A total of 153 patients (75 randomized to lansoprazole and 78 to omeprazole) withdrew prematurely from the study (Fig. 1). The primary reasons for premature discontinuation were as follows: adverse event (lansoprazole 40 patients, omeprazole 30 patients); lack of symptom relief (lansoprazole 10 patients, omeprazole 15 patients); and loss to follow-up (lansoprazole 11 patients, omeprazole 12 patients). Eleven patients (lansoprazole four patients, omeprazole seven patients) did not complete the daily diaries, did not receive a single dose of study drug, or had inappropriate esophagitis grade (grade $<$2) and were therefore excluded from all intent-to-treat analyses. Overall, patient medication compliance was high, with 97% of patients in each treatment group taking $>$90% of their study medication.

Efficacy Analyses

PERCENTAGES OF HEARTBURN-FREE PATIENTS. The percentages of patients who did not report a single episode of heartburn over the treatment period were analyzed. Using this rigorous criterion, a significantly higher percentage of patients in the lansoprazole treatment group recorded no daytime or nighttime heartburn after one dose as compared with patients in the omeprazole group (Fig. 2). Of those treated with lansoprazole, 33% recorded being free of heartburn on day 1 of treatment as compared to 25% of those treated with omeprazole ($p \leq 0.0001$).

During the days 1–3, wk 1, wk 1 and 2, and the entire 8-wk treatment period, significantly higher percentages of patients did not experience a single episode of heartburn in the lansoprazole group as compared to the omeprazole group (Fig. 2).

SUSTAINED RESOLUTION OF HEARTBURN. The cumulative proportion of patients who reached the start of sustained resolution (defined as 7 consecutive days with no heartburn) was calculated for each treatment group. Time to sustained resolution of heartburn was significantly ($p = 0.029$) shorter in the lansoprazole group than in the omeprazole group.

Higher cumulative percentages of those treated with lansoprazole as compared to omeprazole reported sustained heartburn relief at each evaluation time point (Fig. 3). The differences between lansoprazole and omeprazole treatment groups in the cumulative proportions of patients who reached the start of sustained resolution were greater by day 1 (22.9% and 16.9%, respectively), day 3 (41.2% and 35.3%, respectively), day 7 (53.3% and 50.9%, respectively), and day 14 (67.4% and 63.8%, respectively) as com-

Table 2. Characteristics of the Study Population

Variable	Lansoprazole 30 mg Once Daily (n = 1754)	Omeprazole 20 mg Once Daily (n = 1756)
Sex		
Female	43% (747)	44% (772)
Male	57% (1007)	56% (984)
Age (yr)		
Mean (SD)	47.8 (13.8)	46.9 (13.6)
Range	18–89	18–87
Ethnicity		
White	88% (1540)	88% (1539)
African American	5% (87)	5% (84)
Other	7% (127)	8% (133)
Tobacco		
User	25% (437)	28% (497)
Nonuser*	75% (1317)	72% (1259)
Alcohol		
User	55% (973)	56% (983)
Nonuser†	45% (781)	44% (773)
Caffeine		
User	89% (1566)	89% (1567)
Nonuser	11% (188)	11% (189)
H. pylori status‡		
Positive	29% (508/1752)	28% (488/1754)
Negative	71% (1244/1752)	72% (1266/1754)
Esophagitis grade		
0	<1% (1)	0% (0)
1	0% (0)	0% (0)
2	67% (1176)	69% (1206)
3	26% (447)	25% (440)
4	7% (130)	6% (110)
Daytime heartburn		
Mean % of days with heartburn	90%	90%
Severity/day	1.80	1.80
Nighttime heartburn		
Mean % of nights with heartburn	84%§	82%
Severity/night	1.76	1.73

* Includes ex–tobacco users.
† Includes ex–alcohol drinkers.
‡ Two patients in each treatment group had no test results available.
§ $p < 0.05$ as compared with omeprazole-treatment group.

pared to day 28 (77.2% and 76.2%, respectively) and day 56 (84.3% and 83.0%, respectively), for which narrower differences were observed.

PERCENTAGE OF HEARTBURN-FREE DAYS AND SYMPTOM SEVERITY. During days 1–3 of treatment, patients treated with lansoprazole experienced significantly higher percentages of heartburn-free days (Table 3). In all, 56% of days 1–3 of treatment were heartburn-free among those treated with lansoprazole as compared with 49% among those treated with omeprazole ($p < 0.0001$). The average heartburn severity (mean [SD]) among those treated with lansoprazole (0.62 [0.69]) was significantly lower ($p < 0.0001$) as compared with omeprazole (0.74 [0.72]).

During wk 1 of treatment, patients treated with lansoprazole continued to benefit from a significantly greater percentage of days that were heartburn-free as compared to those treated with omeprazole (Table 3). During this period, 66% of days were heartburn-free among those treated with lansoprazole as compared with 62% of days among those treated with omeprazole ($p < 0.0001$). The average severity of daytime heartburn experienced by lansoprazole-treated patients (0.46 [0.57]) was significantly less ($p < 0.0001$) than that experienced by omeprazole-treated patients (0.53 [0.59]).

Lansoprazole continued to provide significantly greater relief of daytime heartburn ($p < 0.001$) during the first 2 wk of dosing and during the entire 8-wk treatment period. The percentage of days that were heartburn-free during these periods were significantly ($p < 0.001$) greater among those patients treated with lansoprazole as compared to those treated with omeprazole, however, the difference between the two treatment groups narrowed during the 8-wk treatment period (Fig. 4).

The average daytime heartburn severity declined from baseline in both treatment groups. However, lansoprazole-

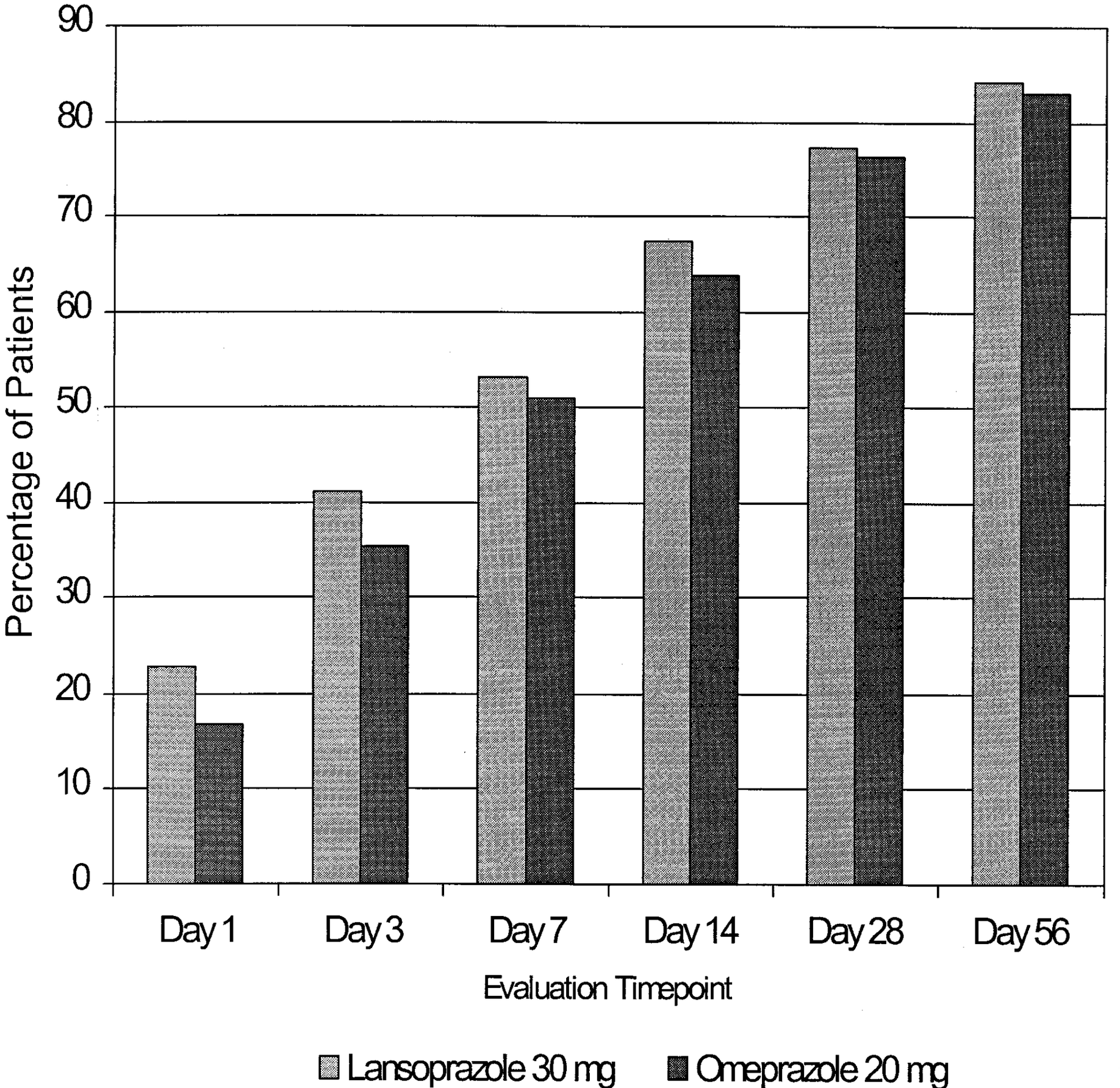
90
80
70
60
50
40
30
20
10
0
Percentage of Patients
Day 1
Day 3
Day 7
Day 14
Day 28
Day 56
Evaluation Timepoint
Lansoprazole 30 mg
Omeprazole 20 mg

Table 3. Summary of Heartburn Data During Days 1–3 and Week 1 Treatment, by Treatment Group

	Lansoprazole 30 mg Once Daily	Omeprazole 20 mg Once Daily
Daytime heartburn during days 1–3 of treatment	n = 1748	n = 1746
Heartburn-free days, %	56%*	49%
Average daytime heartburn severity	0.62*	0.74
Daytime heartburn during week 1 of treatment	n = 1750	n = 1749
Heartburn-free days, %	66%*	62%
Average daytime heartburn severity	0.46*	0.53
Nighttime heartburn during days 1–3 of treatment	n = 1749	n = 1747
Heartburn-free nights, %	60%*	53%
Average nighttime heartburn severity	0.57*	0.70
Nighttime heartburn during week 1 of treatment	n = 1750	n = 1749
Heartburn-free nights, %	69%*	64%
Average nighttime heartburn severity	0.44*	0.51

* $p < 0.0001$ as compared with omeprazole-treated patients.

0.0025) less severe average nighttime heartburn as compared to omeprazole-treated patients during wk 1–2 of treatment (0.37 [0.49] *vs* 0.40, [0.51]) and during the 8-wk period (0.25 [0.41] *vs* (0.27 [0.42]).

EFFICACY ANALYSES BY DEMOGRAPHIC DIFFERENCES. Because there were differences in the baseline parameters of tobacco smoking and the number of nights with heartburn between the treatment groups, all efficacy data were analyzed after stratification for these baseline differences. Results of these analyses were similar to those observed for all patients.

EVALUABLE PATIENT ANALYSES. The results of the analyses performed in the evaluable patient population were similar to those observed in the intent-to-treat population analyses.

TELEPHONE HEARTBURN RECORD ANALYSES. Telephone records confirmed the validity of the patient diaries. Any difference between the patient diary and telephone records was calculated. In all, <6% differences were noted by diary day for either daytime or nighttime heartburn entries in both treatment groups. The results of the analyses

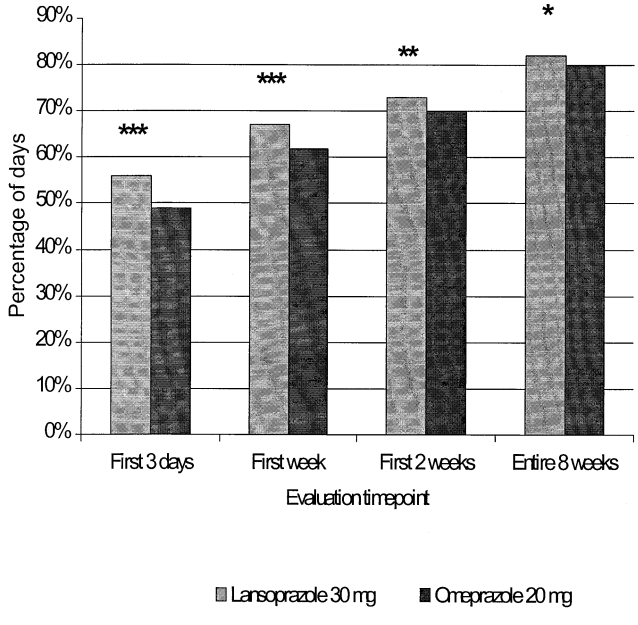

Figure 4. Percentage of heartburn-free days, by treatment group. Lansoprazole provided significantly greater relief of daytime heartburn as compared to omeprazole. During days 1–3, wk 1, wk 1–2, and the entire 8-wk study period, patients treated with lansoprazole reported significantly higher percentages of days that were heartburn-free as compared to those treated with omeprazole. *$p < 0.01$ lansoprazole *vs* omeprazole; **$p < 0.001$ lansoprazole *vs* omeprazole; ***$p < 0.0001$ lansoprazole *vs* omeprazole.

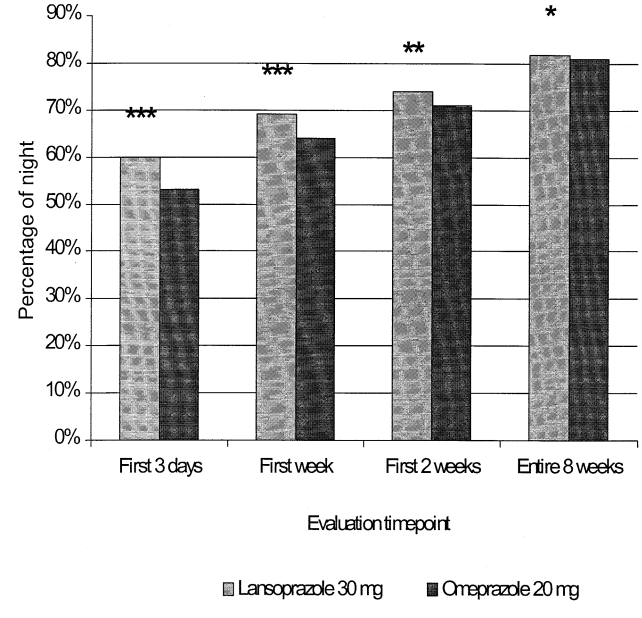

Figure 5. Percentages of heartburn-free nights, by treatment group. Lansoprazole provided significantly greater relief of nighttime heartburn as compared to omeprazole. The percentage of nights that were heartburn-free were significantly greater among patients treated with lansoprazole as compared to those treated with omeprazole during days 1–3, wk 1, wk 1–2, and the entire 8-wk study period. *$p < 0.01$ lansoprazole *vs* omeprazole; **$p < 0.001$ lansoprazole *vs* omeprazole; ***$p < 0.0001$ lansoprazole *vs* omeprazole.

of the percentage of heartburn-free days and the percentage of heartburn-free nights during days 1–3 of treatment using telephone records were similar to those using patient diaries.

Adverse Events

The majority of adverse events were mild or moderate in severity, and the incidence was identical between the treatment groups (44%). Statistically significant differences ($p \leq 0.05$) were observed between the treatment groups for the incidence of diarrhea (lansoprazole 10%, 174/1754; omeprazole 8%, 131/1755), increased appetite (lansoprazole 0.3%, 6/1754; omeprazole 0%, 0/1755), melena (lansoprazole 0.1%, 2/1754; omeprazole 0.7%, 13/1755), and asthma (lansoprazole 0.4%, 7/1754; omeprazole 0%, 0/1755). Each of these events except diarrhea was reported by <1% of the patients in either treatment group.

The mean time (SD) to the onset of diarrhea in the lansoprazole group was 16.1 (1.2) days compared to 11.6 (1.2) days for the omeprazole group. This difference was statistically significant ($p < 0.05$). Most instances of diarrhea were mild or moderate in severity, were self-limited (≤5 days duration), and resulted in few discontinuations. Of the patients who discontinued the study because of adverse events, diarrhea caused eight of 40 lansoprazole patients and three of 33 omeprazole patients to discontinue.

DISCUSSION

The ubiquitous symptom of heartburn profoundly affects those who experience it on a chronic basis. The presence of heartburn results in impairment of work-related activities and general overall well-being (2–4, 21–23). In addition, recurrent heartburn may be associated with a wide range of pathological findings. Although up to one-half of individuals with chronic heartburn have esophageal mucosa of normal appearance, others have varying degrees of esophageal erosions, strictures, or other complications. Unfortunately, it is impossible to predict esophageal pathology or the risk of further injury to the esophageal mucosa simply by assessing patients' symptoms.

The early relief of symptoms, however, allows patients to resume their normal functions of daily living and sleep patterns. Therefore, pharmacological regimens that provide rapid and effective suppression of acid secretion and symptom relief are the mainstay of therapy. Of the agents currently available, proton pump inhibitors are superior to histamine-2 receptor antagonists in relieving symptoms and healing injured tissue. However, because of differences in the pharmacokinetic profiles of each of the respective proton pump inhibitors, the agents may differ in their onset of symptom relief. The bioavailability of lansoprazole is high (approximately 85%) after the first dose and remains so with repeated administration, whereas the bioavailability of omeprazole is approximately 40% after the initial dose and rises to approximately 65% with repeated administration.

The results of this large-scale (>3500 patients), double-blind, multicenter United States study, performed in a population with symptomatic (moderate to very severe heartburn) and endoscopically confirmed erosive esophagitis, confirms that heartburn relief is faster with lansoprazole 30 mg than with omeprazole 20 mg. Significantly higher percentages of lansoprazole-treated *versus* omeprazole-treated patients reported heartburn-free days and nights, lower daytime and nighttime heartburn severity, as well as sustained resolution of heartburn, a commonly used outcome parameter, with initial treatment. The significantly greater efficacy of lansoprazole as compared to omeprazole continued throughout the 8-wk treatment period.

After one dose, a statistically significant difference was observed between the two treatment groups, with a higher percentage of lansoprazole-treated patients recording no daytime or no nighttime heartburn. Approximately 30% more patients were free from daytime and nighttime heartburn (576 of 1747 *vs* 443 of 1747) after one dose of lansoprazole as compared to one dose of omeprazole. The higher bioavailability of lansoprazole may, at least in part, explain the more rapid onset of symptom relief that was observed in our study.

The superior efficacy of lansoprazole in heartburn relief continued during days 1–3 and during wk 1 of continuous administration. Statistically significantly higher percentages of heartburn-free days were reported by lansoprazole-treated patients throughout days 1–3 and wk 1 of treatment (56% and 66%, respectively) as compared with omeprazole-treated patients (49% and 62%, respectively). Throughout days 1–3 and wk 1 of treatment, the percentages of heartburn-free nights reported by lansoprazole-treated patients were also significantly greater as compared to those treated with omeprazole (60% *vs* 53% during days 1–3 and 69% *vs* 64% during wk 1 of treatment). Not unexpectedly, when daily diary data during wk 1–2 treatment and during the entire 8-wk study period were evaluated, the differences in heartburn relief among the two treatment groups narrowed; however, significantly greater effects were still observed in those treated with lansoprazole than those treated with omeprazole.

The severity of heartburn symptoms also was significantly less with lansoprazole as compared with omeprazole after only 1 day of treatment. The intensity of the heartburn symptoms experienced by patients treated with lansoprazole continued to be significantly less during each evaluation time point as compared to those in the omeprazole group.

The overall incidence of adverse events was identical in each treatment group. Each of the events that was statistically significantly different between treatment groups, except diarrhea, was reported by <1% of the patients in either treatment group. A slightly higher incidence of diarrhea was reported for lansoprazole-treated patients (10%) than for omeprazole (8%).

Our finding that lansoprazole produces higher rates of symptom relief than omeprazole was consistent with those of a recent meta-analysis by Huang *et al.* colleagues (19);

however, the differences in this study were more dramatic, with significantly higher efficacy rates observed in lansoprazole-treated patients on treatment day 1 as well as during days 1–3 and wk 1 of dosing. In the meta-analysis by Huang *et al.* (19), a trend was noted in all studies toward higher percentages of patients treated with lansoprazole, as compared with omeprazole, reporting symptom relief after 1–2 wk of treatment.

We believe that the clinical strength and value of this study lies in the measurement of the percentages of patients who were completely heartburn free (*i.e.*, did not report a single episode of heartburn over the treatment period). Using this rigorous outcome parameter, these findings confirm that lansoprazole not only provides greater percentages of patients more complete relief of heartburn symptoms with initial therapy (*i.e.*, after one dose) but maintains its significantly higher efficacy as compared to omeprazole throughout the 8-wk treatment period. This analysis is bold because, when patients have been on proton pump inhibitors and get relief, they tend to revert to behaviors that may exacerbate gastroesophageal reflux and its symptoms. Given the potentially deleterious effect of chronic heartburn, attaining a sustained and complete heartburn-free state may not only provide patients with symptom relief but may also provide maximal esophageal healing protection against future injury.

It is clear that all proton pump inhibitors provide high rates of symptom relief in patients with acid-related disorders. However, patient expectations and satisfaction with their treatment may be highly dependent on how quickly relief is achieved and sustained, allowing them to return to their normal daily activities and level of functioning. The study findings of greater symptom relief early in treatment and for the entire 8-wk course of therapy suggests that higher levels of patient satisfaction are likely to occur with lansoprazole than with omeprazole treatment. Although the significant findings of this study may be at least partially explained by the large number of patients treated, one need only treat 14 patients to see this benefit. However, it remains to be seen whether our study findings are of clinical importance to physicians and patients. They should be interpreted by clinicians in the context of the chronic nature of heartburn, the pathological damage it may produce, as well as the impact of symptoms on patients well-being and quality of life. These results merit consideration when clinicians are prescribing proton pump inhibitors.

In conclusion, lansoprazole 30 mg once daily was more effective than omeprazole 20 mg once daily in eliminating heartburn after one dose as well as after 8 wk of treatment. Relief of heartburn was faster and greater with lansoprazole 30 mg as compared to omeprazole 20 mg. Both treatments were well tolerated.

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Reprint requests and correspondence: Joel E. Richter, M.D., Chairman, Department of Gastroenterology, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Desk S-40, Cleveland, OH 44195.

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APPENDIX

The following individuals contributed to the study as participating investigators: Dennis Avner, Salt Lake City, UT; Paul J. Ballinger, Wenatchee, WA; Charles F. Barish, Raleigh, NC; William R. Berry, Longmont, CO; Thomas D. Bianchi, Tallassee, AL; Leonard Bielory, Newark, NJ; Charles Birbara, Worcester, MA; Phillip C. Bird, Norman, OK; Aleyda Borge, Cooper City, FL; Alin V. Botoman, Ft. Lauderdale, FL; Steven C. Bowman, Clearwater, FL; Randall Elliott Brand, Omaha, NE; Milan L. Brandon, San Diego, CA; Sarah J. Brendler, Springfield, OR; Donald L. Bruns, Red Wing, MN; Donald R. Campbell, Kansas City, MO; Antonio Caos, Ocoee, FL; Amitabh Chak, Cleveland, OH; Gene Chiao, Indianapolis, IN; Roberto Chiprut, Los Angeles, CA; Roland Bernhard Christian, Green Bay, WI; Hollis Clark, Murray, KY; Charles L. Colip, Portland, OR; Bruce Corser, Cincinnati, OH; Douglas D. Dalke, Lincoln, NE; Robert A. Davenport, Lexington, KY; Matthew Davis, Rochester, NY; Carlos de La Garza, Hickory, NC; Mike G. Delissio, Cary, NC; Caroline T. Diamant, La Jolla, CA; Ben J. Dolin, Peoria, IL; David W. Dozer, Greenfield, WI; Sam Jacob Elsheikh, La Mesa, CA; David S. Estock, Wilmington, DE; Axel Feller, North Chicago, IL; M. Brian Fennerty, Portland, OR; Scott D. Fenske, Milwaukee, WI; Chester L. Fisher Jr., Newport News, VA; Duane D. Fitch, Wilson, NC; Stephen Fitzgerald, Winston-Salem, NC; Christopher E. Forsmark, Gainesville, FL; Fred C. Fowler, Charlotte, NC; Almena L. Free, Anniston, AL; Stephen R. Freeman, Denver, CO; Syam Gaddam, Garden Grove, CA; Robert Ganz, Minneapolis, MN; Joseph E. Geenen, Milwaukee, WI; Harry I. Geisberg, Greer, SC; Larry I. Gilderman, Pembroke Pines, FL; Oliver Gilliam, South Bend, IN; Gary S. Gossen, San Antonio, TX; Russell Graham, Altamonte, FL; William L. Gray, Spokane, WA; Martin Greene, Seattle, WA; John W. Hamilton, Madison, WI; William V. Harford, Dallas, TX; Vernon Hee, Vancouver, WA; Charles B. Herring, Wilmington, NC; Basil I. Hirschowitz, Birmingham, AL; Karl Houglum, Spokane, WA; Colin W. Howden, Chicago, IL; David S. James, Tulsa, OK; Vikram S. Jayanty, Houston, TX; James V. Jones Jr, Ruston, LA; Peter J. Kahrilas, Chicago, IL; Robert D. Kaplan, Greensboro, NC; Neil M. Kassman, Statesville, NC; Phillip O. Katz, Philadelphia, PA; C.W. Kessler, Annandale, VA; Chung H. Kim, Rochester, NY; Phillip K. Kiyasu, Portland, OR; Thomas C. Klein, Wichita, KS; Ross A. Kommor, Marietta, GA; Thomas O. G. Kovacs, Los Angeles, CA; George Koval, Portland, OR; Richard A. Krause, Chattanooga, TN; Jay A. Ladenheim, Sunnyvale, CA; Frank L. Lanza, Houston, TX; Robert J. Lapidus, Wheat Ridge, CO; Jake C. Lennard, Amarillo, TX; Susan M. Lepinski, Madison, WI; Michael S. LeVine, Austell, GA; Robert S. Lipetz, Spring Valley, CA; Tom Loludice, Akron, OH; Frank P. Maggiacomo, Cranston, RI; Henry N. Maimon, Dayton, OH; Thomas C. Marbury, Orlando, FL; Paul N. Maton, Oklahoma City, OK; Aubrey D. McElroy, Johnson City, TN; Peter B. Meier, Minneapolis, MN; James M. Mertesdorf, Wilmington, NC; David Colin Metz, Philadelphia, PA; Philip B. Miner Jr., Oklahoma City, OK; James Sill Morgan, Asheville, NC; David J. Morin, Bristol, TN; Morry Moskovitz, Beaver, PA; Samuel Moussa, Tucson, AZ; Rao V. Movva, Moline, IL; William Mroczek, Falls Church, VA; J. Kent Nelson, Bountiful, UT; Diane Normandin, Clearwater, FL; James S. Novick, Towson, MD; William Oetgen, Silver Spring, MD; Michael T. Oliver, Covina, CA; Douglas H. Orchard, Boise, ID; Daniel J. Pambianco, Charlottesville, VA; Peter M. Pardoll, St. Petersburg, FL; Naynesh Patel, Kettering, OH; David A. Peura, Charlottesville, VA; Alan J. Plotner, Lansdowne, VA; John W. Popp Jr., West Columbia, SC; David C. Pound, Indianapolis, IN; Albert J. Razzetti, DeLand, FL; Adisesha B. Reddy, Tuscaloosa, AL; Michele Reynolds, Dallas, TX; Joel E. Richter, Cleveland, OH; Lee R. Rocamora, Winston-Salem, NC; Andres Rodriguez, Tallahassee, FL; John D. Rowekamp, Winona, MN; Lance A. Rudolph, Albuquerque, NM; Dennis Anthony Ruff, San Antonio, TX; Michael Safdi, Cincinnati, OH; Julio Salcedo, Norfolk, VA; Gilberto Sanchez, Montgomery, AL; Colleen Schmitt, Chattanooga, TN; David J. Schneiderman, Carmichael, CA; Timothy T. Schubert, Tacoma, WA; David Schulman, Burbank, CA; Howard I. Schwartz, Miami, FL; Jerrold L. Schwartz, Arlington Heights, IL; Michael E. Schwartz, Jupiter, FL; Ronald Schwarz, Raleigh, NC; Charles W. Scowcroft, Anderson, SC; Atul Shah, Prince Frederick, MD; Umedchandra K. Shah, Hollywood, MD; Stephan C. Sharp, Nashville, TN; B.N. Shivakumar, Davenport, IA; Gerard Siciliano, Louisville, KY; Ann L. Silverman, Royal Oak, MI; David R. Silvers, Metairie, LA; William J. Snape, Jr., Long Beach, CA; Steven C. Solik, Durham, NC; Stephen Sontag, Hines, IL; Harry Sperber, St. Petersburg, FL; Douglas J. Sprung, Maitland, FL; Joseph Staffetti, New Port Richey, FL; Jawahar Taunk, Palm Har-

bor, FL; Thomas G. Tietjen, Cheyenne, WY; James D. Torosis, Redwood City, CA; Mitchel Scott Touger, Birmingham, AL; Bradley A. Towbin, West Palm, FL; Krishna Tripuraneni, Loxahatchee, FL; Brian van der Linden, Salem, VA; William Watkins, Gastonia, NC; David L. Williams, Daytona Beach, FL; John A. Winder, Sylvania, OH; Peter Winkle, Cypress, CA; Barry D. Winston, Houston, TX; James C. Wolper, Fort Meyers, FL; Frank Taylor Wootton III, Norfolk, VA; Lawrence D. Wruble, Memphis, TN; and Marc J. Zuckerman, El Paso, TX.