Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett’s high-grade dysplasia

Bergein F. Overholt, MD, Kenneth K. Wang, MD, J. Steven Burdick, MD, Charles J. Lightdale, MD, Michael K immey, MD, Hector R. Nava, MD, Michael V. Sivak, Jr, MD, Norman Nishioka, MD, Hugh Barr, MD, Norman Marcon, MD, Marcos Pedrosa, MD, Mary P. Bronner, MD, Michael Grace, PhD, Michelle Depot, PhD, on behalf of the International Photodynamic Group for High-Grade Dysplasia in Barrett’s Esophagus

Knoxville, Tennessee, Rochester, Minnesota, Dallas, Texas, New York, Buffalo, New York, Seattle, Washington, Cleveland, Ohio, Boston, Massachusetts, USA, Gloucester, United Kingdom, Toronto, Ontario, Edmonton, Alberta, Mont-Saint-Hilaire, Quebec, Canada

Background: Barrett’s esophagus (BE) with high-grade dysplasia (HGD) is a risk factor for development of esophageal carcinoma. Photodynamic therapy (PDT) with Photofrin (PHO) has been used to eliminate HGD in BE.

Objective: Our purpose was to compare PHOPDT plus omeprazole with omeprazole only (OM).

Design: Five-year follow-up of a randomized, multicenter, multinational, pathology-blinded HGD trial.

Setting: 30 sites in 4 countries.

Patients: 208.

Interventions: Patients with BE and HGD were randomized (2:1) to PHOPDT (n = 138) or OM (n = 70) into a 2-year trial followed up for 3 more years. PHOPDT patients received 2 mg/kg PHO intravenously followed by endoscopic laser light exposure of Barrett’s mucosa at a wavelength of 630 nm within 40 to 50 hours to a maximum of 3 courses at least 90 days apart. Both groups received 20 mg of OM twice daily. Pathologists at one center assessed biopsy specimens in a blinded fashion.

Main Outcome Measurement: HGD ablation status over 5 years of follow-up.

Results: At 5 years PHOPDT was significantly more effective than OM in eliminating HGD (77% [106/138] vs 39% [27/70], P < .0001). A secondary outcome measure preventing progression to cancer showed a significant difference (P = .027) with about half the likelihood of cancer occurring in PHOPDT (21/138 [15%]) compared with OM (20/70 [29%]), with a significantly (P = .004) longer time to progression to cancer favoring PHOPDT.

Limitations: Not all patients were available for follow-up.

Conclusions: This 5-year randomized trial of BE patients with HGD demonstrates that PHOPDT is a clinically and statistically effective therapy in producing long-term ablation of HGD and reducing the potential impact of cancer compared with OM. (Gastrointest Endosc 2007; 1:3-13.)

Adenocarcinoma of the esophagus and gastroesophageal junction is the most rapidly increasing cancer (in percentage terms) in western societies.1 Barrett’s esophagus (BE) is a premalignant condition of the esophagus, increasing the risk of developing adenocarcinoma of the esophagus at least 40 times greater than the normal population.2-4 Most authorities adhere to the progression of BE with no dysplasia, to low-grade dysplasia, to high-grade dysplasia (HGD), and then ultimately to esophageal adenocarcinoma.5,6 The time course of this neoplastic progression is not clearly defined, but HGD in BE is a major risk factor for development of esophageal adenocarcinoma.5,7,8 Treatment of BE has focused on medication, surveillance, esophagectomy, and endoscopic ablative therapies. Endoscopic ablative therapies such as photodynamic
therapy (PDT) and thermal ablation with laser, argon plasma coagulation, or multipolar electronic coagulation are techniques having varying degrees of success in causing regression or reversal of BE and to a limited degree, ablation of HGD. A phase III multicenter, multinational, randomized, pathology-blinded trial with appropriate sample size examined the objectives of both eradication of HGD and potential reduction in occurrence of cancer. Results showed a significant difference in favor of the group being treated with porfimer sodium (Photofrin [PHO]) plus PDT along with omeprazole (PHOPDT) compared with omeprazole only (OM) in both ablation of HGD and occurrence of cancer. The initial report of this trial summarized the findings in patients followed up for 2 years by use of strict entrance criteria and rigid external monitoring techniques. As part of the original trial protocol, there was the opportunity for patients to continue for 3 additional years. Although the 2-year results provided evidence allowing for the granting of regulatory approval of PHOPDT in the ablation of HGD in BE, the long-term follow-up addressed concerns relative to the longer-term durability of the treatment, specifically as to whether the positive results at 2 years would be maintained over time.

METHODS

This 5-year follow-up represents the continuation of the multicenter, multinational, pathology-blinded, randomized phase III trial in patients with HGD in BE. Ethics approval was granted at 30 sites at the beginning of the trial, and patients provided informed consent. All patients who completed the first 2 years of the trial according to protocol were eligible for follow-up. Patients and trial physicians were aware of the treatment each patient received, but pathologists who read the biopsy specimens from each endoscopy were blinded to treatment and patient identification. In the long-term phase of the trial, patients remained in the same randomized treatment group centrally assigned at the beginning of the initial 2-year phase. All histologic assessments were carried out at an internationally recognized central reference laboratory.

Criteria

The patient inclusion criteria at the initial phase of the trial were as follows: diagnosed BE with HGD, central laboratory biopsy-proven HGD in BE, 18 years of age and older, and a signed consent. Women of childbearing potential had to practice acceptable birth control and have a negative urine pregnancy test. Exclusion criteria were as follows: cancer other than nonmelanoma skin cancer within the last 5 years; prior PDT to the esophagus; esophageal strictures unresponsive to dilation; esophageal ulcers >1 cm diameter; esophageal or gastric varices; contraindications to analgesia or endoscopy; class III/IV cardiovascular disease; acute or chronic significant illness; OM therapy contraindicated; known porphyria or porphyrin hypersensitivity; blood cell count, <2.5 × 10^9/L; platelet count, <50 × 10^9/L; hemoglobin, <90 g/L; hematocrit, <27%; normalized ratio of prothrombin time >1.5 upper normal limit; serum creatinine >1.5 upper normal limit; serum bilirubin >1.5 upper normal limit; and aspartate aminotransferase or alanine aminotransferase or alkaline phosphatase >2.5 upper normal limit.

Patients in the PHOPDT arm received a maximum of three PDT courses over 5 years, with courses of PDT separated by at least 3 months. An endoscopic surveillance and biopsy protocol follow-up approach was undertaken to assess long-term efficacy of the treatment. One course of PDT consisted of a 2.0 mg/kg PHO injection followed by one laser light session (630 nm wavelength) applied to the esophageal segment with HGD at 40 to 50 hours after injection. The light dose was 130 J/cm of diffuser length with the centering balloon. A second light application of 50 J/cm without the centering balloon could be given 96 to 120 hours after PHO injection, but only to treat areas showing insufficient mucosal response after the first light application (“skip” areas). A maximum of 7 cm of BE was treated during one course of PDT. It was required that the entire length of Barrett’s mucosa be treated with PDT.

Patients in both treatment groups received OM (20 mg twice daily).

Research design

The initial phase of the trial required a minimum of 24 months of follow-up after randomization of the last patient. The long-term phase of the trial was planned to provide further assessment of therapy for an additional 3 years. Patients were assessed for efficacy (histologic review of biopsy specimens) and safety (adverse events [AE], laboratory results, and physical examinations). Patients progressing to cancer or undergoing intervening therapy were classified as treatment failures and were
removed from the study; endoscopic surveillance was no longer required.

**Treatments**

PHOPDT is a regulatory approved combination drug-device treatment for HGD in BE; it is a 2-stage process, first requiring intravenous injection of PHO, and, second, administration of laser light. Patients who received PHO were photosensitive and had to observe precautions to avoid exposure of eyes and skin to direct sunlight and high intensity visible light for at least 30 days. They were also instructed to wear dark sunglasses for a 30-day period when outdoors.

**Blinding**

Pathologists evaluating biopsy specimens were blinded to treatment assignment and patient identification.

**Measurements**

Relevant medical history with regard to previous disease (other than BE) or other abnormality was documented. Underlying medical conditions present (other than BE) before trial entry were recorded. Conditions that became worse were reported as an AE.

Endoscopy with mucosal assessment and biopsies was performed at the first visit and every 3 months until 4 consecutive quarterly follow-up endoscopic biopsy results were negative for HGD and then biannually until 60 months of follow-up evaluations after randomization or until treatment failure. Mucosal assessment provided an endoscopic mechanism for describing mucosa of the esophagus at specific distances from the dental margin. Each endoscopy involved mapping Barrett’s mucosa and visual identification of abnormal esophageal tissue. Distal (gastric fold) and proximal (squamocolumnar junction) margins of Barrett’s mucosa and diaphragmatic narrowing were measured relative to distance from the dental margin. Endoscopy length was measured as a categorical variable. Presence or absence of hiatal hernia, nodules, ulcerations, and strictures was assessed. Location of hiatal hernia and distal and proximal margins of stricture or ulcer, development of a stricture, use of dilation, and outcome of procedure were noted.

Four-quadrant large particle biopsies every 2 cm of the original length of BE were performed. Biopsy specimen length was measured as a categorical variable. Chromoendoscopy staining of mucosa was used as appropriate to identify additional locations of Barrett’s metaplasia for biopsy specimens. Biopsies at levels of previous HGD diagnosis and all areas suspicious for carcinoma, including nodules, were also performed.

A CT scan of the thorax and an EUS were performed within 14 days if a follow-up biopsy specimen was positive for cancer. These assessments could be outside the time window of ±10 days.

Any AE was recorded: date of onset, event intensity (mild, moderate, severe), relationship to treatment (none, unlikely, possible, probable, definite or unknown), date of resolution, action taken (none, study termination, concomitant medication, procedure), seriousness, and outcome (resolved, improved, unchanged, worsened, death, lost to follow-up).

For patients who discontinued the PHOPDT arm, AEs were recorded for a 90-day period after the last PHO injection or for 30 days after the last biopsy, whichever was longer. For patients who discontinued from OM, AEs were recorded for 30 days after the last biopsy. Esophageal ulcers or strictures observed during endoscopy were assessed relative to baseline. An increase in intensity or the onset of new events was assessed as an AE.

**Efficacy**

Primary efficacy was complete ablation of HGD. A responder was a patient who achieved complete ablation of HGD at any of the 5-year follow-up evaluations. A patient who had complete ablation of HGD and entered a remission period but later relapsed to have HGD recur was still classified as a responder. For each patient who received intervening therapy, assessment for primary efficacy was considered a treatment failure from the day intervening therapy began.

Secondary efficacy variables were duration of complete ablation of HGD, time to progression to cancer, rate of progression to cancer, and survival time. Duration of complete ablation of HGD was defined as days from documentation of ablation until day of recurrence of HGD (progression) or progression to cancer. Time to progression to cancer was defined as days from randomization until the date of the first documented progression to cancer. Survival time was measured in days beginning from randomization to death. For patients with no confirmed final date for these 3 parameters, the information used in the data set for censoring purposes was the day the patient was last known to participate or the day intervening therapy began.

**Analysis**

Demographic and clinical characteristics were summarized and compared between groups at baseline for the intent-to-treat (ITT) population with use of the Wilcoxon rank sum and Fisher exact tests. Complete ablation of HGD rates at follow-up visits month 6, 12, 18, 24, 30, 36, 42, 48, 54, and 60 were calculated for each group. Proportion of complete ablation of HGD at each visit was compared between groups with the Fisher exact test. The Kaplan-Meier method estimated survival curves for each group and the log-rank test was used to compare survival curves between the 2 groups. It is recognized that there was multiple testing of outcome data arising from individual patients; however, it is noted that correction by the Bonferroni method (where P values on the order of \( P < .005 \) are
not counted in the correction) would not have removed statistical significance from any of the findings.

Sample size

The sample size used in this trial stems from those remaining eligible patients after 2 years of the initial phase of the trial. The sample size at the outset of the initial phase of the trial provided adequate power for both primary hypotheses addressing complete ablation of HGD and time to progression to cancer.

RESULTS

A summary of the patient disposition is presented in Table 1. A total of 485 patients were screened for inclusion criteria for the trial. There were 208 patients enrolled in the trial according to a 2 (PHOPDT):1 (OM) ratio.

Initial phase withdrawals

Of the patients in PHOPDT withdrawn, the reasons were as follows: 18 (13%) cancer progression, 19 (14%) HGD progression, 2 (1%) death, and 18 (13%) other. Of the patients in OM withdrawn, the reasons were as follow: 20 (29%) cancer progression, 20 (29%) HGD progression, 1 (1%) death, and 9 (13%) other.

Long-term phase withdrawals

Of the patients in PHOPDT withdrawn, the reasons were as follow: 3 (6%) cancer progression, 1 (2%) HGD progression, and 3 (6%) other. Of the patients in OM withdrawn, the reasons were as follow: 1 (8%) HGD progression and 2 (15%) other.

Long-term enrollment

There were 48 PHOPDT and 13 OM patients enrolled in the long-term phase of the trial as a consequence of withdrawals.

There was no significant difference between the 2 groups at baseline for either the initial or long-term phases with regard to demographic characteristics, medical history, and underlying medical conditions (Table 2). There was also no significant difference between the 2 groups regarding BE characteristics at either the initial or long-term baseline phases (Table 3).

Ablation of HGD

The main outcome was based on analysis of complete ablation of HGD (responders) in the PHOPDT and OM groups in the ITT population during 5 years after randomization (Table 4). The proportion of responders was significantly higher ($P < .0001$) in PHOPDT (106/138 [77%]), 95% CI (0.70-0.84) compared with OM (27/70 [39%], 95% CI 0.27-0.50). Of the responders there were 28 of 106 (26%) PHOPDT and 14 of 27 (52%) OM patients
who terminated the trial with either HGD or cancer. Analysis of responders for both treatment groups at 10 specific time points (6, 12, 18, 24, 30, 36, 42, 48, 54, and 60 months of follow-up) showed a proportion of responders almost twice as great in PHOPDT compared with OM at all assessment periods. From 24 months onward no additional changes were observed in the proportion of responders because only one patient received a PHOPDT course (staying within the protocol limit of a maximum of 3 courses) during continuation of the follow-up until 5 years. There was a significant difference (\( P < .0001 \)) between the median time to complete response of 113 days (95% CI 99-185) in the PHOPDT group and 551 days (95% CI 367, upper limit could not be estimated) in the OM group. Over the trial period 10% of PHOPDT patients had HGD compared with 31% of the OM patients. Figure 1 illustrates the distribution of the duration of response to PHOPDT and OM for complete ablation of HGD. The duration of response after 5 years of follow-up did not differ from that obtained after 2 years. By the end of the 5-year follow-up period, the probability of maintaining complete ablation of HGD was 48% in PHOPDT compared with 4% in OM, which was significantly different (\( P < .0001 \)). The median duration of the complete response was 44.8 months (95% CI 15.1, upper value could not be estimated) in the PHOPDT group and was 3.2 months (95% CI 3.0-5.8) in the OM group. A 2-year responder in the PHOPDT group has a 90% chance of maintaining the response for 5 years compared with 30% for a 2-year responder in the OM group.

**Extent of HGD**

The proportion of responders was significantly higher (\( P = .004 \)) in PHOPDT (92%) with HGD single level compared with those in OM (63%). For patients with HGD multiple levels, the proportion of responders in PHOPDT (70%) was significantly higher (\( P < .0001 \)) than in OM (23%).

**Time to progression to cancer**

Figure 2 provides a display of the time to progression to cancer and shows at what point in time the differentiation between the 2 groups started to occur. Comparison between curves of the 2 groups showed a significant difference (\( P = .004 \)). Patients in PHOPDT had a significant delay in progression to cancer compared with OM.

**Progression to cancer**

In PHOPDT, 21 patients (15%) progressed to cancer from days 48 to 1793. Of the 21 patients, 9 were HGD responders to ablation whereas 12 were nonresponders. In OM there were 20 patients (29%) who progressed to cancer from days 63 to 1092. Of the 20 patients, 1 was an HGD responder to ablation whereas 19 were nonresponders. After 5 years of follow-up, the rate of patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Initial phase group (n = 208)</th>
<th>Long-term phase group (n = 61)</th>
<th>No. (% of patients)</th>
<th>P value*</th>
<th>No. (% of patients)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y [SD])</td>
<td>PHOPDT (n = 138)</td>
<td>OM (n = 70)</td>
<td>66 (11)</td>
<td>67 (11)</td>
<td>.34</td>
<td>PHOPDT (n = 48)</td>
</tr>
<tr>
<td>Sex (n [%])</td>
<td>Male</td>
<td>117 (85)</td>
<td>59 (84)</td>
<td>&gt; .99</td>
<td>PHOPDT (n = 48)</td>
<td>OM (n = 13)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>21 (15)</td>
<td>11 (16)</td>
<td>7 (15)</td>
<td>2 (15)</td>
<td></td>
</tr>
<tr>
<td>Race (n [%])</td>
<td>White</td>
<td>137 (&gt; .99)</td>
<td>68 (97)</td>
<td>.41</td>
<td>PHOPDT (n = 100)</td>
<td>OM (n = 100)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>0</td>
<td>1 (1)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>1 (&lt;1)</td>
<td>1 (1)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Smoking history (n [%])</td>
<td>Current user</td>
<td>8 (6)</td>
<td>8 (11)</td>
<td>.14</td>
<td>2 (4)</td>
<td>2 (15)</td>
</tr>
<tr>
<td></td>
<td>Former user</td>
<td>85 (62)</td>
<td>47 (67)</td>
<td>30 (62)</td>
<td>9 (69)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Never user</td>
<td>44 (32)</td>
<td>15 (21)</td>
<td>16 (33)</td>
<td>2 (15)</td>
<td></td>
</tr>
</tbody>
</table>

NA, Not available.

*Wilcoxon rank sum test for continuous variables and Fisher exact test for categorical variables.
who progressed to cancer in PHOPDT was significantly lower \( (P = .027) \) than in OM.

### Survival time

Two patients in PHOPDT and 1 patient in OM died within the first 2 years from events that were not related to Barrett’s disease and no deaths were related to the treatment. There were no additional patients who died over the course of the additional 3 years of follow-up. These deaths were accounted for in the analysis.

### Safety

In the initial phase of the trial, the most common PHOPDT events were photosensitivity and esophageal strictures. All photosensitivity events were resolved and 94% of patients with strictures were stricture free during the course of the initial phase.

During the second phase of the trial, from 2 to 5 years, there were no AEs of any serious or severe consequence, and of those AEs reported none were attributed to the treatments. Three patients had an intermittent stricture event during the long-term phase. At the last 5-year endoscopic assessment, the 3 patients had been stricture free for the past 11, 8, and 6 months, respectively. There were no photosensitivity AEs occurring in the long-term phase.

### DISCUSSION

This report presents the long-term 5-year results of the first multicenter, international, randomized, pathology-blinded trial designed to evaluate safety and efficacy of an ablative treatment on HGD in patients with BE using strict endoscopic and biopsy surveillance. The trial was powered for 2 co-primary objectives: assessment of the
5-year efficacy of ablation of HGD in BE and time to progression to cancer using PHOPDT compared with OM. The secondary objectives were to assess duration of response, occurrence of cancer, and survival time. Primary objectives were assessed on the basis of biopsy-proven HGD ablation and cancer.

The long-term phase confirmed results from the initial phase,\textsuperscript{39} that PHOPDT is significantly superior to OM in obtaining complete ablation of HGD. The long-term phase did not allow additional PDT treatment, hence favoring a potential for OM to improve the proportion of responders during the continuation phase compared with the PDT group. There were no new cases of ablation during the long-term phase in either group, resulting in no change in the proportions of ablation. The lack of change in the proportion of responders to OM over the 5-year follow-up confirms the limitation of OM as potential treatment. This result is supported by the durability of HGD ablation when using PHOPDT, which was also significantly better than in OM at both 2-year and 5-year follow-ups. The effect of PHOPDT relative to OM was maintained throughout the 5-year trial in spite of no additional treatment being allowed on the basis of the protocol requirements.

Time to progression to cancer in PHOPDT was significantly prolonged compared with OM. As a secondary objective over the 5-year follow-up period, results showed that PHOPDT continued to be significantly superior to OM in preventing progression to esophageal cancer, with about half the likelihood of cancer occurring in PHOPDT (15%) compared with OM (29%). In summary, PHOPDT produced HGD ablation, durability of ablation, and reduction of cancer occurrence relative to OM.

Photosensitivity reactions and esophageal strictures were the most consequential reported adverse events from the initial phase of the trial and have been described previously.\textsuperscript{39} No long-term effects of esophageal strictures or photosensitivity reactions were found at the time of the 5-year analysis. Three patients continued with strictures from the initial 2-year phase but were asymptomatic by the end of the long-term trial.

About 60% of both groups consented to continue through the long-term phase of the trial. However a much larger percentage of the PHOPDT group was eligible to continue than in the OM group 2 years after randomization, which reflects fewer failures in the PHOPDT group during the initial phase. Patients who did not continue were lost to follow-up, relocated, believed that regular endoscopic surveillance was not needed, felt their disease condition did not warrant further care, or their sites declined further participation. The reasons for sites not continuing in the study ranged from investigator relocation, an unwillingness to submit to another ethics approval process on the basis of a minimal number of patients appropriate for follow-up, no more eligible patients remaining, or unavailability of a nurse coordinator.

No statistically significant difference was found between

\begin{table}[h]
\centering
\caption{5-Year clinical response}
\begin{tabular}{lccc}
\hline
 & PHOPDT & OM & \(P\) value* \\
\hline
Patients (n) & 138 & 70 & \\
Complete HGD ablation (CR) & 106 & 27 & \\
Proportion 95% CI & 0.77 (0.70-0.84) & 0.39 (0.27-0.50) <.0001 & \textbackslash
\hline
\end{tabular}
\end{table}

\*Fisher exact test.

Figure 1. Comparison by group of duration of HGD ablation.

Figure 2. Comparison by group of time to progression to cancer.
patients continuing in the long-term phase of the trial and those not continuing in terms of demographics, baseline clinical features, and outcome characteristics. Consequently, patients remaining in the long-term phase adequately reflect those patients enrolled in the initial phase of the trial. No more than 3 courses of PHOPDT were allowed in the trial, so it is not known whether additional courses of PHOPDT would have provided new findings. PHOPDT was a single modality treatment; no other modality was used in the trial.

Although esophagectomy was not a comparator group, it is useful to make general comparisons. The mortality rate for esophagectomy ranges from 8.4% (very high volume institutions) to 20.3% (very low volume institutions) adjusted mortality rates for the procedure.40 The mortality rate for esophagectomy is much higher than that observed in both PHOPDT and OM groups in this 5-year trial. Only 3 patients in the trial died (2 PHOPDT and 1 OM), all from non-BE diseases, with none being treatment-related. Esophagectomy also leads to significant morbidity, such as wound infections, anastomotic leaks, and cardiovascular complications.41 Barrett's epithelium may also develop in the esophageal remnant after esophagectomy.42

Given the positive HGD ablation and cancer reduction shown by PHOPDT in this trial relative to OM and according to standards of evidence-based medicine, PHOPDT should be considered as a potential first-line therapy in BE patients with HGD.

PHOPDT is the only nonsurgical option for treating HGD in BE patients that meets evidence-based criteria (such as strict entry criteria, properly estimated sample size, randomization, multicenter and multinational, pathology team blinded to identity and group, and both short- and long-term positive results).45 Other trials of endoscopic ablation of HGD in BE did not meet similar evidence-based standards because they usually involved a mixture of LGD and HGD conditions, limited sample size, single center or only several center studies, fewer methodologic criteria applied, and less-extensive follow-up.8-37

There were limitations to the trial that was originally developed and conducted. The ideal trial might have had 3 arms randomized to compare esophagectomy versus PHOPDT versus OM. However, ethical and methodologic objections arose when such a trial was suggested, leading to the decision to compare PHOPDT with OM.

The fact that neither patients nor clinicians were blinded to the treatment can potentially bias results (including safety), but given the treatment involved it was difficult to create any form of sham application of PHOPDT. However, bias is unlikely because the primary outcomes were assessed by a team of pathologists blinded to personal identity and treatment and did not involve personnel who were directly involved with patients.

Results of this 5-year trial clearly indicate that PHOPDT (in conjunction with omeprazole) is a statistically and clinically effective endoscopic therapy for eliminating HGD in patients with BE and delaying onset of cancer compared with OM.

ACKNOWLEDGMENTS

The contribution and effort of the site coordinators is appreciated. Thanks are extended to Stephanie Leyva of STATPROBE Inc for data management and Rolland Gaudet of Quintiles Canada Inc for statistical analysis. Special thanks go to the DSMC for overseeing the conduct of the study.

DISCLOSURE

Each site received grant support from Axcan for the trial. Dr Overholt has a copatent on the esopagheal balloon used in the study. Dr Wang has had some limited consultancy with Axcan in the past but none in the last 2 years. Dr Burdick received honorariums for doing education courses for Axcan; the amount was less than $5000. Dr Marcon has received fees for CME presenting and also owns a small number of shares of Axcan. Dr Grace was involved in the statistical analysis and interpretation of results of the trial and reporting and received consulting fees for this and other Axcan projects. Dr Depot is an employee of Axcan and receives a salary. She also has a minimal number of shares of stock of Axcan. Drs Lightdale, Kimmey, Nava, Sitvak, Barr, Nishioka, Barr, Pedrosa, and Bronner have reported no issues.

REFERENCES


