

## Photodynamic Therapy (PDT) for Advanced Esophageal Cancer

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**Clinical Area:** Photodynamic therapy for esophageal cancer  
**Keywords:** photodynamic therapy, PDP, esophageal cancer, dysphagia, porfimer sodium  
**Reference:** Lightdale CJ, Heier SK, Marcon NE, et al. Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd: YAG laser for palliation of esophageal cancer: a multicenter randomized trial. *Gastrointestinal Endoscopy*. 1995;42:507-12.

**Study Type:** Randomized multicenter trial (Phase III, parallel, comparative, open-label)

### Outcomes

- Primary: symptom palliation (change in dysphagia grade relative to baseline)
- Objective tumor response (endoscopically visible tumor, lumen diameter)
- Survival: (time of randomization to time of death)
- Adverse experiences (sunburn, nausea, fever, pleural effusion, esophageal perforation, withdrawal from study because of adverse events, termination of laser session due to adverse events)

### Design

*N* = 236 randomized (218 treated— PDT = 110, Nd:YAG = 108)

*Description of population:* advanced esophageal cancer

*Inclusion criteria:* Patients at 24 centers, patients with biopsy-proven esophageal malignancy with failure to respond to/recurrence of tumor following/refusal of: chemotherapy, radiation therapy, or surgery (advanced esophageal cancer). Approximately 50% of patients with adenocarcinoma and 50% with squamous cell carcinoma. Patients were symptomatic with malignancy-caused dysphagia to solid foods and a Karnofsky performance status of at least 30%.

*Exclusion criteria:* Involvement of tracheobronchial tree, prior treatment with PDT or Nd:YAG laser, current radiation and chemotherapy (prior therapy must have terminated 4 weeks prior to randomization).

*Power:* Not stated.

*Method of randomization:* Computerized randomized schema.

*Intervention:* Comparison of photodynamic therapy (PDT) to Nd:YAG laser therapy for the palliation of advanced esophageal cancer

- Photodynamic therapy: Porfimer sodium was given at a dose of 2 mg/kg by single IV injection over 3-5 minutes. 40-50 hours later, the esophageal cancer was treated using red light with a wavelength of 630 nm provided by a continuous wave argon-pumped dye laser. Total light dose of 300 J/cm of tumor was delivered. The protocol allowed maximum of 3 courses at 1-month intervals.
- Nd:YAG laser therapy: 15-90 W and a pulse duration of 0.5 to 4.0 seconds was delivered by laser with noncontact or contact technique. Repeat Nd:YAG laser sessions could be given if the initial response to therapy was deemed insufficient. A course of laser therapy was deemed complete when the investigator believed that dysphagia had been sufficiently palliated or that further laser treatment would be futile.

*Blinding:* Open label study

*Length of follow-up:* Assessments were made one week after last treatment and at months 1, 2, 3 and 6. Survival was measured from time of randomization to time of death. Time to palliation failure was measured from time of randomization until first evidence of lack of symptom palliation, worsening of dysphagia, or toxicity.

*Completeness of follow-up:*

- 110 of 118 patients randomized to PDT (93%) and 108 of 118 patients randomized to Nd:YAG (92%) were treated [patients not treated usually had progressive disease or death in the interval between randomization and planned therapy].
- 38% of PDT patients received a second course; 44% Nd:YAG treated patients received second course
- dropout at one week, approximately 20%
- dropout at one month, approximately 40%

**Validity**

- *Is the study type appropriate for the questions being asked?* Yes.
- *Was the study population typical of patients with this disease?* Yes.
- *Were the treatment/control groups comparable at baseline?* Yes.
- *Was the intervention compared to placebo and/or best accepted intervention?* Yes.
- *Was there compliance with the intervention?* Yes.
- *Was there equal intensity of observation of study and control subjects?* Observational bias possible.
- *Was the process of observation likely to effect the outcome?* Yes.
- *Intention to treat analysis?* Yes.
- *Did conclusions about safety take into account the limited size of the study?* No.
- **Conclusions regarding validity of methods:** Valid study weakened by potential for observation bias and high drop out rates.

**Results**

Table 1. Percentage of responders (at least one-grade response to treatment). N=118 in each treatment group

	Week 1 (%)		Month 1 (%)	
	PDT	Nd:YAG	PDT	Nd:YAG
Responders	44	48	35	29
Two or more grades	19	23	14	14
To normal	18	25	19	11
No Change	25	25	24	23
Worsening	9	5	5	6
Missing	22	22	36	42

Differences between the treatment groups were not statistically significant

Table 2. Objective tumor response (N =118 in each treatment group)

	Week 1 (%)		Month 1 (%)	
	PDT	Nd:YAG	PDT	Nd:YAG
CR + PR	45	40	32*	20
SD	24	22	15	14
PD	3	1	11	14
Missing	28	37	42	52

- Absolute risk reduction (CR plus PR with PDT compared to Nd:YAG) = 12% at one month
- CR = complete responses, PR = partial response, SD = stable decrease, PD = progressive disease
- \* P <0.05

Table 3. Percentage of patients with treatment-associated adverse events where statistical analysis indicated a significant difference between treatment groups

	% PDT (n=110)	% Nd:YAG (n=108)
Sunburn	19 *	0
Nausea	8 *	2
Fever	16 *	5
Pleural effusion	10 *	2
Esophageal perforation	1	7

- There was no difference between treatment groups in death during the study period
- \* P< 0.05

### Authors' Conclusions

Photodynamic therapy is an effective method for palliation of esophageal cancer. It's efficacy overall is equivalent to Nd:YAG thermal ablation therapy for relief of dysphagia. Mild and moderate side effects are more common after PDT than Nd:YAG laser therapy (most notably, patients are at temporary risk for sunburn). Severe adverse events occur with equal frequency except for perforation which is more common after Nd:YAG laser therapy. PDT is a more comfortable treatment for patients and is technically easier to perform. PDT seems to be particularly appropriate for situations in which Nd:YAG laser therapy is difficult because of tumor morphology or location.

### Reviewers' Conclusions (Mike Stuart, MD, Matt Handley, MD)

Photodynamic therapy when compared to Nd:YAG thermal ablation for palliation of dysphagia from advanced esophageal cancer provides equivalent improvement in dysphagia, improved objective tumor response as measured by esophageal lumen diameter (ARR of 12% at one month in "complete response + partial response" P <0.05), and increased mild to moderate complications including sunburn in 19% of patients treated with PDT. Perforations from laser treatments or associated dilatations occurred in 1% of patients following PDT and 7% of patients following Nd:YAG treatment. (p<0.05) Termination of laser sessions due to adverse events occurred in 3% of patients receiving PDT and 19% receiving Nd:YAG. While this is an RCT, the high drop out rate and lack of blinding limit our ability to understand the difference in clinically important outcomes between Nd:YAG thermal ablation and PDT.

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11/16/99