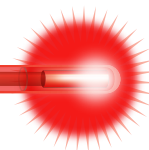


# Achieving Clinically Proven Treatment Results With Photodynamic Therapy (PDT) and PHOTOFRIN® (porfimer sodium)



## PHOTOFRIN® (porfimer sodium) IS INDICATED FOR

Palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy. Treatment of microinvasive endobronchial non-small cell lung cancer (NSCLC) in patients for whom surgery and radiotherapy are not indicated.

Reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial NSCLC.

PHOTOFRIN® (porfimer sodium) is indicated for the ablation of high-grade dysplasia (HGD) in Barrett's esophagus patients who do not undergo esophagectomy.

## IMPORTANT SAFETY INFORMATION ABOUT PHOTOFRIN FOR INJECTION

Photodynamic therapy (PDT) with PHOTOFRIN is a two-stage process requiring administration of both drug and light in a properly equipped facility. Refer to the OPTIGUIDE® instructions for use for complete instructions concerning the fiber optic diffuser.

PHOTOFRIN is contraindicated in patients with porphyria. PDT is contraindicated in patients with an existing tracheoesophageal or bronchoesophageal fistula and patients with tumors eroding into a major blood vessel. PDT is not suitable for emergency treatment of patients with severe acute respiratory distress caused by an obstructing endobronchial lesion because 40 to 50 hours are required between injection with PHOTOFRIN and laser light treatment. PDT is not suitable for patients with esophageal or gastric varices, or patients with esophageal ulcers >1 cm in diameter.

Tracheoesophageal or bronchoesophageal fistula can occur if esophageal tumor is eroding into trachea or bronchial tree. Gastrointestinal perforation can occur. There is a high risk of bleeding in patients with esophageal varices and for fatal massive hemoptysis with endobronchial tumors that are: large, centrally located; cavitating; extensive, extrinsic to the bronchus. After treatment of high-grade dysplasia (HGD) in Barrett's esophagus (BE), monitor endoscopic biopsy every three months, until four consecutive negative evaluations for HGD have been recorded. Photosensitivity can be expected; ocular sensitivity is possible. Allow 2-4 weeks between PDT and subsequent radiotherapy. Substernal chest pain may occur after treatment. Treatment-induced inflammation can cause airway obstruction. Administer with caution to patients with tumors in locations where treatment-induced inflammation can obstruct the main airway. Esophageal stenosis occurs frequently after treatment of HGD in BE. Patients with hepatic or renal impairment may need longer precautionary measures for photosensitivity (possibly more than 90 days). Thromboembolic events can occur following photodynamic therapy with PHOTOFRIN.

**MOST COMMON ADVERSE REACTIONS** reported during clinical trials are:

**Esophageal Cancer:** Anemia, pleural effusion, pyrexia, constipation, nausea, chest pain, pain, abdominal pain, dyspnea, photosensitivity reaction, pneumonia, vomiting, insomnia, back pain, pharyngitis.

**Obstructing Endobronchial Cancer:** Dyspnea, photosensitivity reaction, hemoptysis, pyrexia, cough, pneumonia.

**Superficial Endobronchial Tumors:** Exudate, photosensitivity reaction, bronchial obstruction, edema, bronchostenosis.

**High-Grade Dysplasia in Barrett's Esophagus:** Photosensitivity reaction, esophageal stenosis, vomiting, chest pain, nausea, pyrexia, constipation, dysphagia, abdominal pain, pleural effusion, dehydration.

Inform patients to report adverse reactions. All patients who receive PHOTOFRIN will be photosensitive for at least 30 days and should be warned about this and counselled to take appropriate precautions. Laser treatment should not be given if an overdose of PHOTOFRIN is administered.

**FOR MORE INFORMATION ABOUT PHOTOFRIN** visit [www.Photofrin.com](http://www.Photofrin.com) or call Concordia Laboratories Inc. at 1-877-370-1142.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.

Please see full prescribing information for PHOTOFRIN.



**PDT WITH  
PHOTOFRIN®**  
(porfimer sodium) for Injection

**Light up the possibilities**

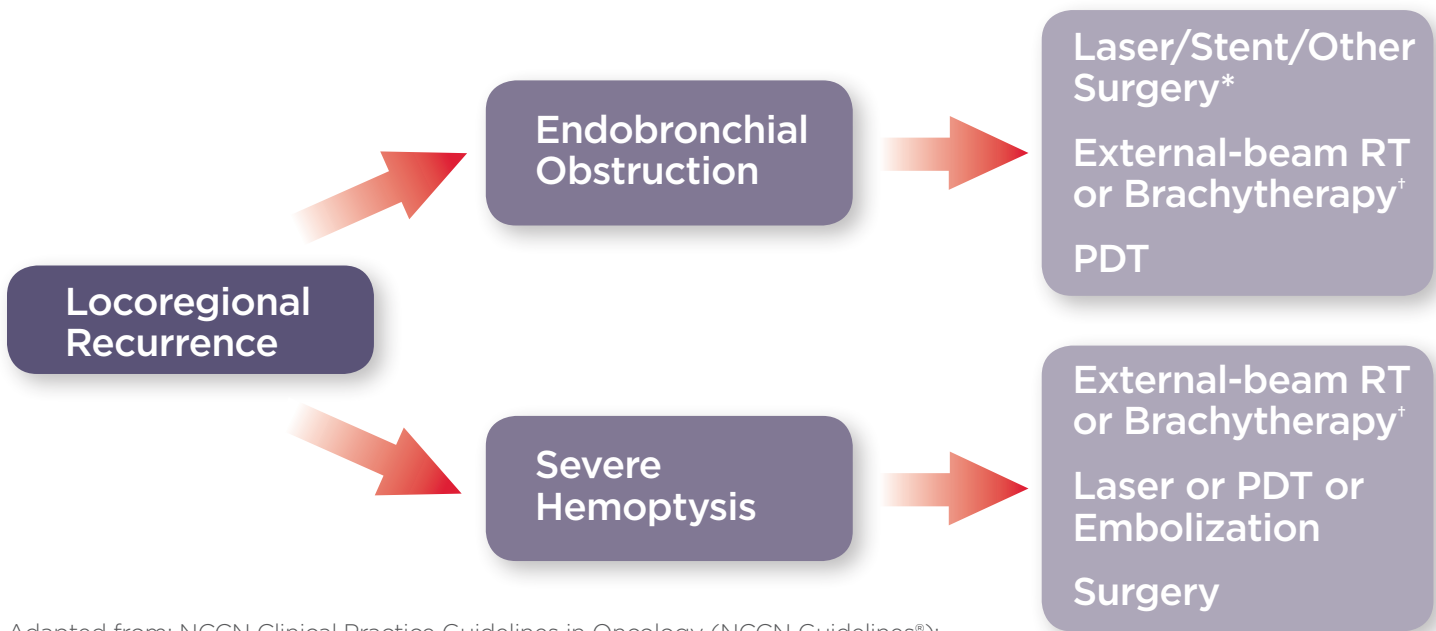
# Photodynamic Therapy (PDT) Is a Guideline-Recommended Endobronchial Therapy<sup>1</sup>

PDT is one of the most studied endobronchial treatment modalities.<sup>2</sup>

## PDT IN DIFFERENT STAGES OF NON-SMALL CELL LUNG CANCER (NSCLC)

- It is one of the modalities for definitive therapy for carcinoma *in situ* and microinvasive (superficial) NSCLC<sup>3</sup>
- Symptomatic management Stage I or II<sup>4,5</sup>
- Can be used for induction for Stage IIIA or IIIB<sup>5</sup>
- Palliation<sup>6</sup>

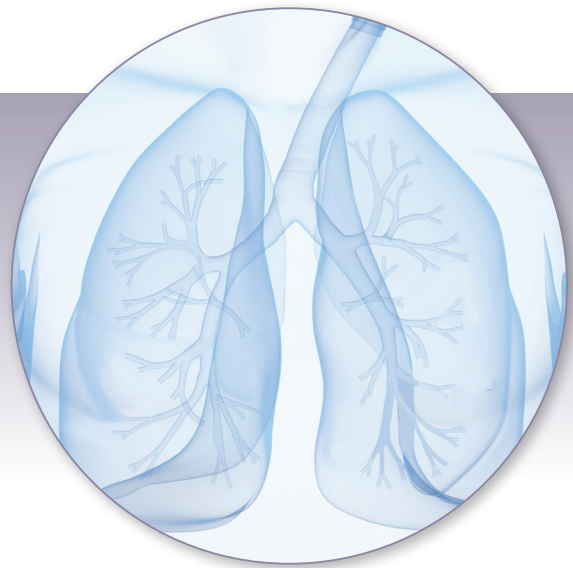
## THERAPY FOR RECURRENCE<sup>1</sup>



Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer. Version 7.2015.

\* See Principles of Surgical Therapy (NSCL-B).

† See Principles of Radiation Therapy (NSCL-C).



References quoted may have used settings not within the prescribing information for PHOTOFRIN® (porfimer sodium).

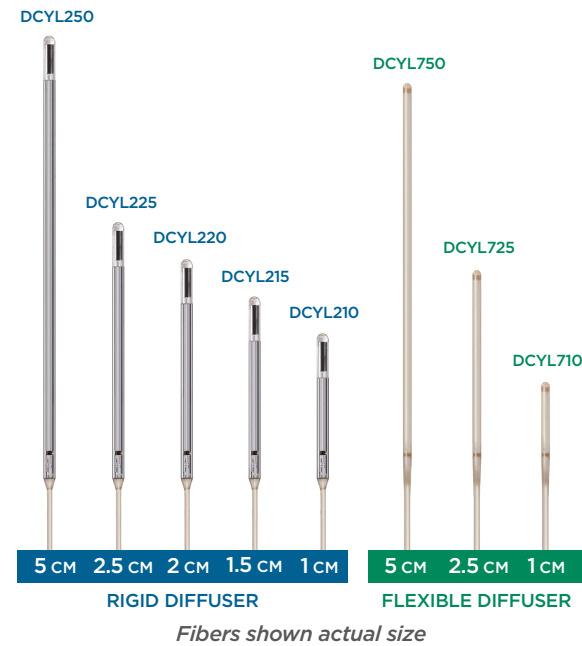
# The 3 Components of Photodynamic Therapy (PDT)

## 1. PHOTOFRIN® (porfimer sodium)

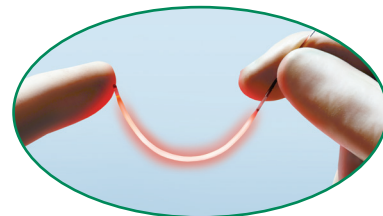


PHOTOFRIN (porfimer sodium) is injected 40-50 hours prior to laser activation and is selectively retained in tumor cells. When activated with red laser light, the drug produces a chain reaction of cell death in targeted tissue.

## 2. FIBER



The OPTIGUIDE® Diffuser Series features a range of fibers for reaching the tumor and delivering red laser light for PHOTOFRIN activation. The Diffuser Series includes the rigid DCYL200 series and the DCYL700 series, featuring new flexible-yet-durable material to ease navigation through instruments and anatomy.



DCYL700 DIFFUSER SERIES

**OPTIGUIDE® FIBER OPTIC**  
**DCYL200**  
CYLINDRICAL  
DIFFUSER SERIES

**OPTIGUIDE® FIBER OPTIC**  
**DCYL700**  
CYLINDRICAL  
DIFFUSER SERIES

## 3. LASER



The laser generates red light with a wavelength of 630 nm to activate PHOTOFRIN.

**DIOMED**  
630 PDT LASER

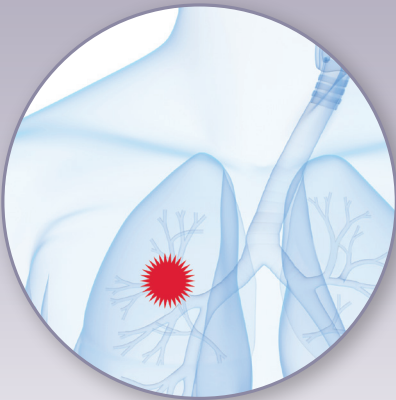
**PDT WITH PHOTOFRIN®**  
(porfimer sodium) for Injection  
Light up the possibilities

DAY 1



ADMINISTRATION

Typically used in an outpatient setting, PHOTOFRIN (porfimer sodium) is reconstituted and administered as a single IV injection over 3 to 5 minutes.



TARGETED RETENTION

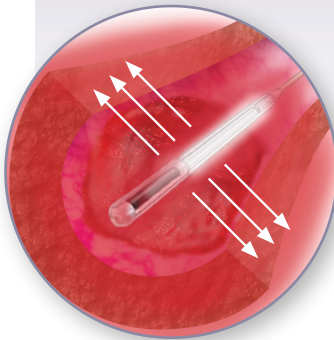
Photosensitizer is selectively retained in cancer cells.

DAY 3



LASER APPLICATION

An OPTIGUIDE® Fiber Optic Diffuser is used to administer 630 nm nonthermal light.



Excited PHOTOFRIN (porfimer sodium) causes vasoconstriction, which leads to vascular occlusion and additional tumor cell death.<sup>7</sup>

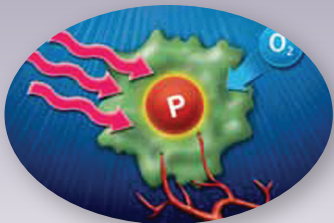
DAY 5

DEBRIDEMENT

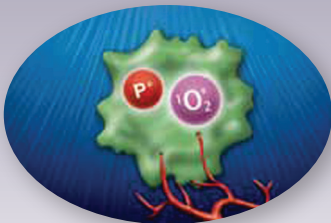
Removal of post treatment necrotic tissue.



ACTIVATION



Red light permeates tissue (the indicated light dosimetry for endobronchial cancer is 200 J/cm) and activates PHOTOFRIN to an excited state.<sup>7</sup>

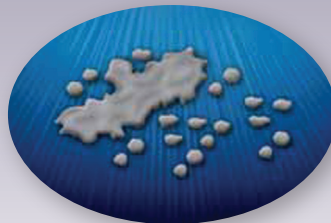


Energy transfer generates reactive singlet oxygen<sup>7</sup> and selective necrosis of the target lesion up to a 6-mm depth.<sup>8</sup>

DESTRUCTION OF CANCER CELLS



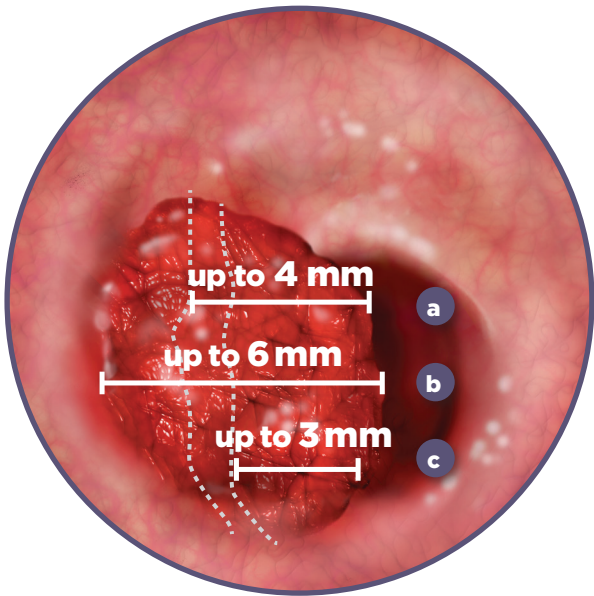
Excited PHOTOFRIN causes vasoconstriction, which leads to vascular occlusion and additional tumor cell death.<sup>7</sup>



Treatment results in lysis and ischemic necrosis of cancer cells.<sup>7</sup> Cleanout bronchoscopy is performed to remove obstructive debris.

# PDT Makes Selective Treatment of Target Lesions and Tumor Margins Possible Up to a Depth of 6 mm<sup>8</sup>

Photodynamic therapy (PDT) provides depth of ablation—up to 6 mm.



- a** Cryotherapy
- b** PDT PHOTOFRIN® (porfimer sodium)
- c** Argon Plasma (30-90W)

## ESTIMATED DEPTH OF DAMAGE FOR VARIOUS METHODS OF ENDOSCOPIC MUCOSAL ABLATION<sup>8</sup>

Method of ablation	Approximate depth of ablation (mm)	Author/ref
Argon laser (514 nm)	0.3	Weston 2003
KTP laser (532 nm)	0.4	Dix 1996
Diode laser (805 nm)	1.3	Dix 1996
Nd:YAG laser (1064 nm)	4–6	Dix 1996
APC (30–90 W)	1–3	Barham 1996 Franchimont 2003
MPEC 15–20 W	1.7–4.8	Sampliner 2003
ALA PDT	2	Tan 1999 Gossner 1990
Exogenous PDT	4–6	Barr 1990 Heier 1995
Cryotherapy	1–4	Johnston 2003

KTP, potassium titanyl phosphate; Nd:YAG, neodymium yttrium aluminium garnet; APC, argon beam plasma coagulation; MPEC, multipolar electrocoagulation; ALA PDT, 5-aminolevulinic acid photodynamic therapy.

# Benefits of Photodynamic Therapy (PDT)

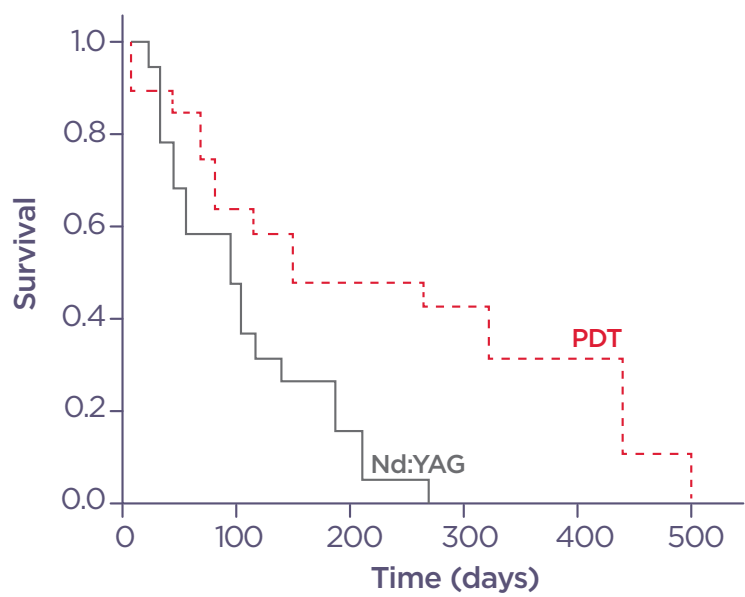
## TUMOR RESPONSE AND ATELECTASIS IMPROVEMENT<sup>7</sup>

Efficacy results from studies in late-stage obstructing endobronchial cancer—all randomized patients\*

Efficacy parameter	PDT N=102, % patients	Nd:YAG N=109, % patients
Objective tumor response <sup>†</sup>		
Week 1	59%	58%
Month 1 or later	60%	41%*
Atelectasis improvement <sup>‡</sup>		
	n=60	n=71
Week 1	35%	18%
Month 1 or later	35%	20%

\* Statistical comparisons were precluded by the amount of missing data at Month 1 or later (e.g., for tumor response, PDT 28% missing, Nd:YAG 38%).  
<sup>†</sup> CR+PR where CR=complete response (absence of bronchoscopically visible tumor) and PR=partial response (increase of ≥50% in the smallest luminal diameter; or any appearance of a lumen for completely obstructing tumors).  
<sup>‡</sup> In patients with atelectasis at baseline.

## EXTENDED SURVIVAL AND SYMPTOM IMPROVEMENT COMPARED TO ND:YAG LASER RESECTION<sup>9</sup>



Probability of survival of patients with inoperable non-small cell lung cancer (NSCLC) assigned to photodynamic therapy (---) and Nd:YAG laser resection (—).

- Fourteen patients out of 31 with late-stage obstructing endobronchial cancer who were treated with PHOTOFRIN® (porfimer sodium) PDT achieved:
- Post treatment survival was significantly longer in the PDT group than in the Nd:YAG laser resection group: 265 days PDT, 95 days Nd:YAG,  $P=0.007$
  - Similar improvement in dyspnea, cough, hemoptysis symptoms and sputum production in both groups



Benefits of Photodynamic Therapy (PDT)

IMPROVED PERFORMANCE STATUS AND RESPIRATORY FUNCTION<sup>6</sup>

Stage IIIA-IV Symptom Palliation in Patients With Advanced Inoperable Bronchogenic and Endobronchial Luminal Obstruction

Changes in Bronchial Luminal Obstruction, Pulmonary Ventilation, and Performance Status Following Treatment With PDT<sup>6\*</sup>

Parameters	Pre PDT Mean±SD	Post PDT Mean±SD	Changes
% Obstruction	85.8±19.6	18.5±17.3	-67.3%
(% Range)	(30-100)	(0-35)	
FVC (1) L	2.07±0.78	2.50±0.74	+0.43 L
FEV1 (1) L	2.07±0.78	2.50±0.74	+0.43 L
WHO ≤2	N=43	N=87	+44
WHO >2 <sup>†</sup>	N=54	N=10	-44

**WHO performance status scores summary**  
0 - Asymptomatic  
1 - Symptomatic but completely ambulatory  
2 - Symptomatic, <50% in bed during the day  
3 - Symptomatic, >50% in bed, but not bedbound  
4 - Bedbound  
5 - Death  
**44 patients (81% of WHO >2) move to WHO ≤2**

\* Study was prospective nonrandomized.  
† In 3 patients, pretreatment WHO was recorded as between 2 (Symptomatic, <50% in bed during the day) and 3 (Symptomatic, >50% in bed, but not bedbound).



References quoted may have used settings not within the prescribing information for PHOTOFRIN® (porfimer sodium).

Multimodality Treatment With Photodynamic Therapy (PDT)

SEQUENCE AND TIMING OF THERAPIES<sup>7,10\*</sup>

PDT in combination with	Induction/Neoadjuvant	Concurrent	Adjuvant	Comments relating to PDT
Nd:YAG/APC	X	X	X	PDT may be beneficial when utilized after Nd:YAG or APC to further enhance local control <sup>10</sup>
Chemotherapy	X	X	X	Avoid overlapping toxicities <sup>10</sup> Ensure/confirm blood cell count normal <sup>10</sup>
Radiation therapy (XRT, EBRT, SBRT, brachytherapy)	X		X	2-4 weeks if PDT is used prior to radiation <sup>7</sup> 4 weeks if radiation is used prior to PDT <sup>7</sup> The timing of PDT is ideal before radiotherapy because of its potential impact on vascular access <sup>7</sup>
Surgery	X		X	Allow 10-12 weeks post PDT for surgical intervention <sup>10</sup>

\*PHOTOFRIN® (porfimer sodium) prescribing information does not include reference to PDT use in conjunction with other treatment modalities besides radiotherapy.

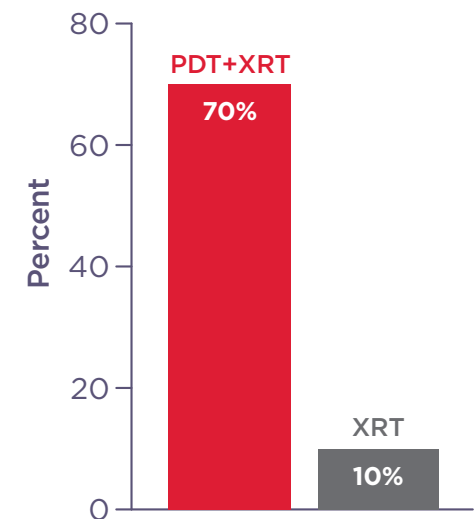


# Radiation Treatment and Photodynamic Therapy (PDT)

PDT MAY BE USED WITH RADIATION THERAPY (XRT), WHICH MAY PROVIDE ADDITIONAL BENEFITS<sup>11</sup>

## Patients With Inoperable Non-Small Cell Bronchogenic Carcinoma Obstructing a Central Airway

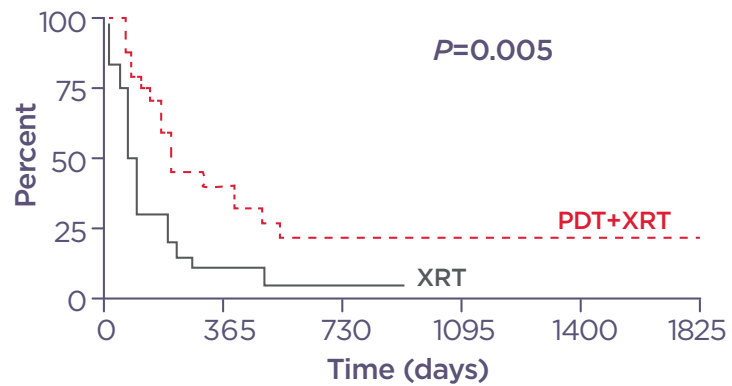
### Complete Reopening of Bronchial Lumen With No Residual Tumor



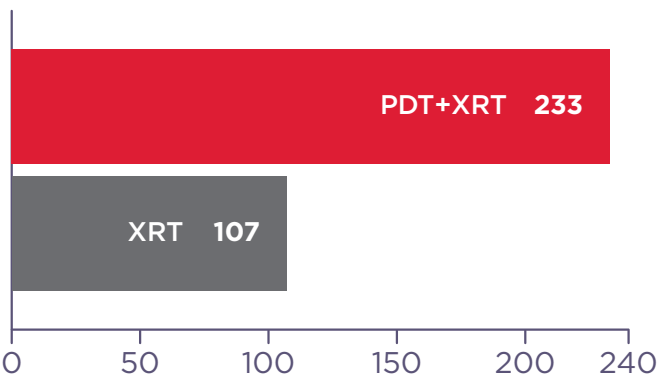
Complete reopening of the bronchial lumen with no gross tumor visible on bronchoscopy was observed in 2 of 21 patients (10%) in the XRT group and 14 of 20 patients (70%) in the PDT+XRT group at 1 and 3 months after treatment ( $P<0.05$ ).

There were no treatment failures in the PDT+XRT group, but 4 of 21 (19%) patients in the XRT group failed to respond to treatment.

### Interval Between Treatment and Local Recurrence



### Median Time to Local Recurrence



The median interval between treatment and local recurrence was significantly longer in the PDT+XRT group than in the XRT group (233 days vs 107 days,  $P=0.005$ ).

Palliation of hemoptysis and shortness of breath was significantly better for the PDT+XRT group 3 months after treatment, along with reduction in cough at 1 and 3 months.

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- On-site assistance to help establish the use of photodynamic therapy (PDT) in your facility
- PDT Laser support
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- Reimbursement and billing support

## FOR YOUR PATIENTS



- Patient education materials
- Patient co-pay assistance
- Referral to independent nonprofit co-pay foundations
- Patient assistance program

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