PHOTOFRIN® (porfimer sodium) for Injection

CASE STUDY: Endobronchial Microinvasive Squamous Cell Carcinoma

Courtesy of Gregory Loewen, DO, FCCP
Associate Professor of Medicine
Washington State University

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 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, or call 1-800-FDA-1088.

Please see full prescribing information for PHOTOFRIN.

PATIENT HISTORY

This 81-year-old male (current smoker) in a CT-based lung cancer screening program presented with severe COPD and asbestos exposure. Although no endobronchial airway lesions were visible, CT detected a suspicious pulmonary nodule in the right upper lobe (Figure 1).

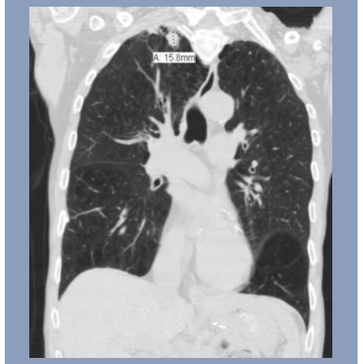


Figure 1

Figure 1 CT imaging confirmed a 15.8-mm adenocarcinoma at the apex of the right lung, seen on coronal image.

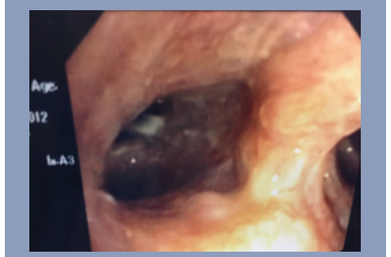
EXAMINATION

The patient reported a chronic cough and admitted to occasional scant hemoptysis. Although he did not use supplemental oxygen, his physical exam revealed diminished breath sounds bilaterally. Pulmonary function testing revealed obstructive disease with an FEV-1 of 1.55 liters (58% predicted) and a DLCO of 27% predicted.

DIAGNOSTIC EVALUATION

CT-guided needle biopsy of the apical right upper lobe lesion confirmed the diagnosis of adenocarcinoma. Surveillance bronchoscopy was recommended prior to therapy. The patient underwent surveillance fiber optic bronchoscopy with white light and autofluorescence technique, which confirmed the presence of endobronchial mucosal nodularity in the left upper lobe (Figure 2) and in the right upper lobe (not shown).

Endobronchial biopsies and brushings were obtained from both the left upper lobe orifice and the right upper lobe orifice, confirming the presence of multifocal microinvasive squamous cell carcinoma in situ (CIS) as synchronous primary lung cancers.



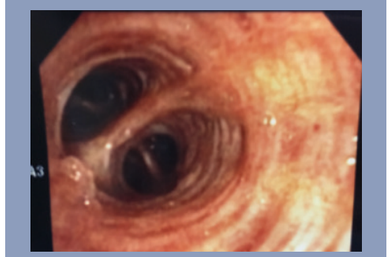


Figure 2

Figure 2 The left upper lobe bronchial orifice mucosa was nodular, mildly erythematous, and friable (left). Friable mucosal nodularity was also noted on the tertiary carina of the right upper lobe orifice (right).

COURSE OF TREATMENT

After review of the patient's case at a multidisciplinary chest tumor board, PET scan revealed fluorodeoxyglucose (FDG) uptake in the right apical lesion and a Standard Uptake Value (SUV) of 10 at the apex of the right lung. No FDG uptake was found in the microinvasive endobronchial squamous cell carcinoma lesions in the orifice of the right upper lobe and left upper lobe (Figure 3).

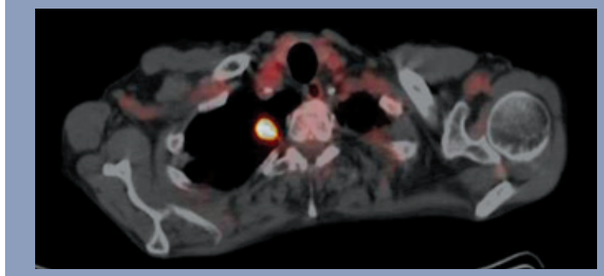


Figure 3

Figure 3 PET image of the right lung, in the area of adenocarcinoma and at the sites of microinvasive endobronchial squamous cell carcinoma. PET slices through right and left upper lobe were negative for FDG uptake.

It was established that the patient had clinical stage 1a adenocarcinoma of the right upper lobe, in concert with 2 stage 0 squamous cell carcinomas in the right upper lobe and left upper lobe orifices. The patient was unwilling to consider surgical resection but agreed to stereotactic body radiotherapy (SBRT) as primary therapy for his adenocarcinoma at the right lung apex, and subsequent photodynamic therapy (PDT) for the 2 airway lesions.

The patient first underwent SBRT in five fractions to the right upper lobe, which was well tolerated. One month later, 2 mg/kg of PHOTOFRIN® (porfimer sodium) was administered intravenously and sunlight precautions were initiated. Forty-eight hours later, bronchoscopy was performed under general anesthesia. Under direct guidance, a 10-mm cylindrical fiber was positioned adjacent to the nodular mucosa in the left upper lobe orifice, which was treated at the energy setting of 200 Joules/cm with a nominal wavelength of 630 nm ±3 nm (Figure 4). Subsequently, the same treatment was performed adjacent to the nodular mucosa in the right upper lobe orifice.

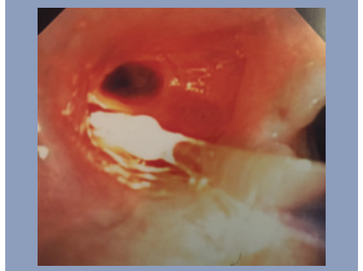


Figure 4

Figure 4 Endoscopy during PHOTOFRIN® (porfimer sodium) treatment adjacent to the area of CIS in the left upper lobe as well as the right upper lobe.

Clean-out debridement bronchoscopy was performed 48 hours later under local anesthesia and monitored sedation. The left upper lobe and right upper lobe orifices were both partially obstructed with white necrotic debris, which was easily removed with forceps. One year post-treatment, mature scar with some discoloration was observed, but biopsies were negative for malignancy (Figure 5).

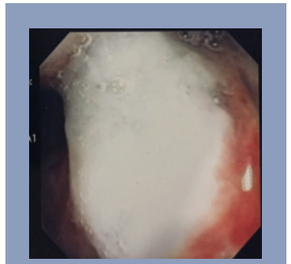
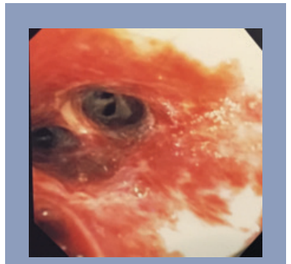


Figure 5



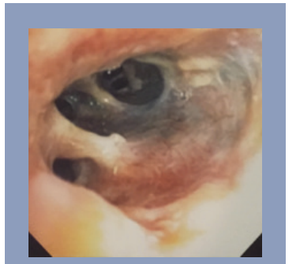


Figure 5 Post-treatment debris is shown in the left upper lobe orifice (left image), which was debrided to expose the erythematous orifice (center image). Mature scar shown 1 year post-treatment (right image).

CLINICAL OUTCOMES

PHOTOFRIN® (porfimer sodium) treatment resulted in a complete pathological response in both the right upper lobe and left upper lobe orifices. Repeat bronchoscopy 1 and 2 years later revealed no evidence of tumor in the airways of either lobes. PHOTOFRIN® treatment, in concert with SBRT, was well tolerated in this patient with severe lung disease, and resulted in a complete pathologic response of the microinvasive squamous cell carcinoma in situ that was durable.

DISCUSSION

PDT with PHOTOFRIN is an established endobronchial therapy for superficial spreading, microinvasive, non–small cell lung cancer, which is typically of squamous cell carcinoma cell types. These lesions may be multifocal, and are frequently metachronous. Advantages of PDT over other endobronchial techniques include the selective photochemical mechanism of action combined with the targeted application of light within the field of cancerization.[1] Squamous cell carcinoma in situ and microinvasive squamous cell carcinoma are important precursors to squamous cell endobronchial lung cancers, and may be detected with advanced bronchoscopy techniques (autofluorescence or narrow-band imaging) in high-risk patients.[2,3] PDT is one of the most studied endobronchial treatment modalities, and we consider it a good option for microinvasive superficial non-small cell carcinoma.[4]

References: 1. Loewen GM, Pandey R, Bellnier D, Henderson B, Dougherty T. Endobronchial photodynamic therapy for lung cancer. *Lasers Surg Med.* 2006;38(5):364-370. **2.** Demmy TL, Loewen GM. Management of superficial central airway lung cancers. In: Sugarbaker DJ, Bueno R, Colson YL, Jaklitsch MT, Krasna MJ, Mentzer SJ, et al eds. Adult Chest Surgery. 2nd ed. New York, NY: McGraw-Hill Education; 2015:706-717. **3.** Jayaprakash V, Loewen GM, Dhillon SS, Moysich KB, Mahoney MC, Yendamuri S, et al. Early detection of lung cancer using CT scan and bronchoscopy in a high risk population. *J Cancer Ther.* 2012;3(4A):388-396. doi: 10.4236/jct.2012.324051. **4.** Wisnivesky JP, Yung RC, Mathur PN, Zulueta JJ. Diagnosis and treatment of bronchial intraepithelial neoplasia and early lung cancer of the central airways: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(5 Suppl):e263S-e277S.

Please see accompanying Important Safety Information within sales aid and full Prescribing Information for PHOTOFRIN® (porfimer sodium).

FOR MORE INFORMATION ABOUT PHOTOFRIN visit 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, or call 1-800-FDA-1088.

Concordia Laboratories Inc. St. Michael, Barbados BB11005

See more at: http://www.photofrin.com/healthcare-professional-home/#sthash.FInUv0e7.dpuf.

If there are any questions regarding the information provided, please contact Concordia's Medical Information Department at 1-877-370-1142.

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

CONCORDIA LABORATORIES INC

PINNACLE BIOLOGICS