Phase I/II clinical trials for skin cancer and advanced esophageal cancer. This chlorin type photosensitizer came out of a large study we carried out to find an optimum photosensitizer among pyropheophorbide ethers, HPPH was found to provide the optimum in vivo photodynamic activity in experimental rodent tumors and in veterinary patients (dogs/cats) and to induce the least normal tissue toxicity. It is activated at 665nm, compatible with existing diode lasers, and is predicted to produce cutaneous photosensitivity in patients for one week or less. These clinical trials will commence in late 1997.

Looking into the future is of course difficult. Certainly the type of information presented by others in this symposium, when widely known, will encourage both physicians and patients to consider PDT. The advent of diode lasers, to be used with Photofrin and other photosensitizers, will make PDT more acceptable to physicians. Some of the newer photosensitizers noted above may induce less cutaneous photosensitivity than does Photofrin, which also will increase the acceptance of this new therapy. However, this cannot be done at the expense of efficacy considering the benign nature of the photosensitivity problem. The real challenge for PDT, however, is to clearly demonstrate its superiority to existing treatments in certain types of cancers (early stage lung and esophageal cancers, for example) and to establish its place in the overall management of cancer patients.

REFERENCES


Photodynamic Therapy for Lung Cancer

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This study describes 41 patients with small lung cancers treated between January 1990 through April 1993, in a non-comparative open-label study. Conditions of treatment were homogeneous because all patients were treated in the same study center with the same laser and by only one investigator. Of the 41 patients, 38 (93%) were male and the average age was 63 years. All of the patients had superficial endobronchial carcinoma. All cases were 18 years age or older and presented histologically-proven inoperable non-small cell lung cancer which was radiologically occult (CIS or TI). The CT scan also failed to display any abnormalities. All lesions were accessible endoscopically.

Other modalities were excluded because of poor pulmonary function, inoperable general condition, recurrent multifocal lesions, failure to respond to conventional therapy or refusal of standard therapy. The majority of patients had only one tumor therapy. The majority of patients had only one tumor (83%) and most cases (81%) were squamous cell carcinoma. These included 6 CIS cases. Most tumors
were located in lobar bronchi (68%) and 70% of the tumours had an area of 1–10 mm². Approximately 50% of the patients had a relevant medical history: respiratory disease (37%), cardiovascular disease (29%) and 26 patients had previously been treated for lung cancer by one or more methods (surgery 20; external beam radiation 8; chemotherapy 5; PDT 2).

Since 1986 we have used the same argon-dye laser (Aurora-Cooper, Mountain View California). All patients were treated with cylindrical diffusing fibers, aiming at a power density of 400 mW/cm². The patient is injected with 2 mg/kg body weight of Photofrin intravenously, 48 hours prior to illumination with non-thermal light of 630 nm wavelength. The treatment is performed under local anesthesia, with a flexible endoscope and routine oxygen support. Usually endoscopy and biopsy are performed on day 4 or day 5 following the treatment with light although endoscopy may be performed earlier if it seems necessary. Generally follow-up endoscopy is performed on day 8, 30 and at 3 months, 6 months, 9 months, and 12 months. The tumor response is classified as either complete response if the histology is negative or, if the biopsy is still positive, as failure. We have been able to follow up for 5 years or more in 27% of cases. The median follow up is 1053 days. Out of the total of 41 patients we have observed CR in 36 cases. The time to tumor recurrence was 588 days with a range from one month to almost 6 years at the time of this report. (Fig. 1)

Out of the 41 patients, 14 died due to the cancer but median disease-specific survival is 4.5 years from the date of injection. The estimated 5-year disease-specific survival rate is 45%. We obtained an 88% overall response rate. PDT is safe. We have observed only 3 cases of skin photosensitivity all of which were due to the patient’s not following instructions, and 9 adverse events, only 2 of which were severe (one needing tracheostomy because of tracheal edema, the other requiring placement of a stent on day 161 due to stenosis in the main bronchus). No treatment-related death occurred.

In conclusion, although it is very difficult to estimate the actual number of patients for whom PDT should be performed, it is possible to say that it is an extremely efficient treatment for small lesions. In certain cases the effects of PDT may be compared to surgery. The development of PDT and the treatment of lung cancer depends on the development of detection systems for early stage lesions. Finally, while certain criticisms can be made about PDT with the drug Photofrin concerning uniformity of light absorption and its photosensitization, nevertheless the fact is that Photofrin is the most widely used photosensitizer in the world and is the only one which has received official sanction. However, the PDT concept does require development beyond Photofrin. This new therapeutic approach can be employed by the chest physician, the thoracic surgeon, and oncologist and it is a very useful and unparalleled weapon in the arsenal of weapons against cancer.