CHEMOTHERAPY FOR LUNG CANCER

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There are a variety of discussions in the field of oncology about different drugs and different levels of drug dosing for treatment of patients with lung cancer. Chemotherapy is frequently used for most lung cancer patients - especially when the cancer has spread locally, regionally or distantly. Frequently it is used in association with radiation. For lung cancers, chemotherapy sensitizes the cancer to the radiation, thus making it more effective.

Some believe that higher doses of chemotherapeutic agents are more beneficial while others suggest that the toxicity is only enhanced. A particular type of lung cancer called small cell defined because of it appearance under the microscope was recently analyzed in a randomized study. Most lung cancers are not oat cell and are, thus named non-small cell as a category. Non-small cell constitutes the majority of lung cancers.

Small cell or oat cell presents in general as two stages. Limited stage means confined to the chest, and extensive stage being beyond the chest cavity.

For patients with limited stage oat cell, radiation and chemotherapy are used. For patients with extensive stage oat cell carcinoma chemotherapy is generally used, at least as initial therapy.

Different regimens have been analyzed in the oncology world including Cyclophosphamide, Doxorubicin, and Vincristine known as CAV or Etoposide and Cisplatin known as EP for patients with extensive stage oat cell carcinoma.

Another regimen using Cisplatin, Vincristine, Doxorubicin and Etoposide, nicknamed CODE, was produced to increase the intensity of drug administration giving four agents at one time rather than two or three days in each cycle with the CAV or EP concoction.

The CODE combination was designed to give more Cisplatin, more Doxorubicin, more Vincristine and more Etoposide over nine weeks compared to the CAV/EP over 18 weeks. CODE regimen left out Cyclophosphamide.

The rationale of this approach was that in the original Canadian study CODE appeared to offer better results than standard therapy.

To enter the study all patients had small cell carcinoma that was extensive in stage, meaning beyond the lung, mediastinum, and supraclavicular lymph nodes.

Patients who had complete response meaning no evidence of cancer anywhere or partial response meaning marked shrinkage of the cancer in the primary site and complete response in all other sites were to receive thoracic radiation and prophylactic brain radiation.

Thoracic radiation was to administer 3000 rad over ten fractions. Rad is a measurement of radiation. The purpose of prophylactic brain radiation was to try to kill microscopic disease potentially present at the brain. Chemotherapy often does not penetrate the blood brain barrier. Patients with oat cell cancer have a relatively high rate of metastases to the brain.

The study started in July 1992 and ended in April 1996. The study was terminated because of toxic deaths on the combination chemotherapy using CODE. Two hundred and twenty patient had been randomized for this study.

Thoracic radiation was given to 27% of the patients after CAVE chemotherapy and to 41% of the patients after CODE therapy. This suggested that the CODE therapy was more effective in

creating responses throughout the body.

However, the toxicity of CODE was greater. Statistical analysis was performed looking at toxicity and indeed found near significant levels.

Fever associated with low white blood count occurred in 17% of patients on CAV-EP and 19% of the patients on CODE. Six patients died on CODE and none on CAV-EP due to infection.

Other causes of death included lack of blood to the heart in one patient on CAV-EP and two patients who had blood clots in the lung after CODE therapy. Additionally, one patient had respiratory distress syndrome and died after CODE chemotherapy.

The complete response rate disappearance of all cancer was 20% for the CAV-EP and 23% for the CODE. The overall response rate, partial or complete disappearance, was 87% for CODE and 70% for CAV-EP. Ten percent of both groups who were free of cancer at ten years, although there was a greater average time of being free of cancer on the CODE than the CAV-EP.

At two years, about 18% of patients were alive. While the likelihood of response was greater, the chance of being free of cancer or being alive was not improved on the more intense chemotherapeutic approach. The authors suggested that this might be because a resistant form of cells develop and causes the patient's demise.

The mortality rate of 8.2% after CODE was felt to be unacceptable compared to the 1% rate on more traditional CAV-EP chemotherapy. The authors felt that the improved survival seen on this study was probably not due to treatment but due to selection criteria that chose patients more likely to endure the intensive treatment approach.

The researchers concluded that, "This study concludes that standard combination chemotherapy protocols that cause moderately severe mild suppression are as efficacious and less toxic than intensive regimens for the treatment of extensive stage small cell lung carcinoma.

It seems improbable that reconfiguration of drugs used in this trial would result in significant improvement for these patients. Although these results do not necessarily contradict trials that have demonstrated improved outcome with more intensive therapy for limited small cell lung cancer patients, confirmatory trials that show worthwhile survival improvement are mandatory to justify increased toxicity in this curable patient population.

Our own approach for newly diagnosed lung cancer patients is to use radiation and chemotherapy as combined modality treatment. Surgery is usually not performed for those with oat cell cancer. On the other hand, surgical resection may play an important part of treatment for those with non-oat or non-small cell lung cancer - the more frequently occurring primary lung cancer. However, our radiation is different from standard in that for those seeking more sophisticated treatment we utilize fractionated body radiosurgery to attack the cancer, boost the dose and minimize adverse effects on healthy surrounding tissues. Most all believe that high doses will produce better local control of lung cancers - and better local control will ultimately produce more cures.