

Genetic Differences May Someday Dictate Treatment and Predict Survival

A recent study funded by the National Cancer Institute found that genetic variations in an individual's ability to repair DNA damage helped predict survival in lung cancer patients who were treated with the common chemotherapy drugs cisplatin (Platinol) or carboplatin (Paraplatin). The findings, if confirmed by larger studies, may help oncologists choose chemotherapy drugs based on the patient's genetic make-up.

"We often see that certain patients with advanced stage non-small cell lung cancer tolerate chemotherapy incredibly well and have excellent resources. On the other hand, many patients tolerate chemotherapy very poorly due to toxicities, or their tumors grow despite the most aggressive treatment," said Sarada Gurubhagavatul, MD, Massachusetts General Hospital. "We suspected that one of the reasons for these differences in outcome has something to do with the genetic make-up of the individual."

The study involved 103 patients diagnosed with stage III or IV non-small cell lung cancer (NSCLC) who were treated with cisplatin or carboplatin. The researchers found that certain variations in the DNA repair genes XPD and XRCC1—which are responsible for correcting mistakes that can occur when DNA is copied in preparation for cell division—were associated with a shortened survival.

In addition, when the researchers compared combinations of variations in both genes, they found that more variations were associated with decreased average survival.

Patients with a total of three variations in the XPD and XRCC1 genes survived an average of 6.8 months, while patients with two variations survived a median of 11 months, and those with one variation survived 16.6 months. Patients with no variation survived an average of 20.4 months.

Researchers have investigated the link between XPD and XRCC1 gene variations in patients with other cancers, particularly those with colorectal cancer. This is the first study to look at variations in these genes in patients with lung cancer.

In another study looking at how a patient's genetic make-up can affect their response to treatment, researchers at the M. D. Anderson Cancer Center have found a set of key genetic markers that may predict whether patients with breast cancer are likely to benefit from a common chemotherapy treatment given before surgery.

"In the past, we have not been able to reliably predict at the time of diagnosis which patients will experience a complete pathologic response to any chemotherapy regimen," said lead investigator Lajos Pusztai, MD, PhD, M. D. Anderson Cancer Center.

The research shows that the genetic markers were 75% accurate in predicting whether chemotherapy would completely eliminate tumor cells in patients with early stage breast cancer treated with a regimen known as T/FAC. T/FAC consists of paclitaxel (Taxol) followed by 5-Fluorouracil (5-FU), doxorubicin (Adriamycin or Rubex), and cyclophosphamide (Cytosan).

"If our results are confirmed by larger ongoing studies, we soon may be able to select the best preoperative chemotherapy regimen for patients based on the gene expression profile of their tumors," said Dr. Pusztai. "This would maximize the chance of curing their disease while sparing them from the toxic side effects of less effective treatments."

While the results are promising, Dr. Pusztai cautioned that they need to be validated in large clinical trials before a test to predict patients' responses to chemotherapy could be routinely used.

What Does This Mean for Patients?

The concept of selecting a chemotherapy drug based on a patient's genetic make-up is relatively new, and not something that is likely to be routinely used to determine treatment for many years to come. However, these findings bring oncologists one step closer to selecting the most effective chemotherapy treatment for individual patients based on their own unique genetic make-up.

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