

WEB EXCLUSIVES

Lung Cancer Patients May Soon Have New Drug Option

BY MELISSA WEBER

A drug temporarily withdrawn from the Food and Drug Administration for approval in non-small cell lung cancer will still likely get the green light when it's resubmitted, Alan Sandler, MD, told a group of medical professionals at the Practical Applications of New Agents in Oncology conference in March in San Antonio, Texas.

Sandler, chief of the division of hematology and medical oncology at Knight Cancer Institute at Oregon Health and Science University, devoted a portion of his presentation on new drugs for NSCLC to Erbitux (cetuximab) and the research study included in the approval application. (Lung cancer would be the third cancer to join the approved indications for Erbitux, behind colorectal cancer and head and neck cancer.)

The phase III FLEX trial, reported at last year's annual meeting of the American Society of Clinical Oncology, compared the chemotherapy combination of cisplatin and vinorelbine with or without Erbitux as initial treatment for advanced NSCLC. Overall survival reached 11.3 months for patients receiving Erbitux plus chemotherapy compared with 10.1 months for patients receiving chemotherapy alone. The time before the disease progressed was the same for both groups, reaching 4.8 months. The most common side effects of Erbitux included low blood counts and rash.

The numbers separated dramatically, however, when the researchers looked at responses in Asians versus whites. Sandler shared the FLEX investigators' slides, which showed median overall survival reached 19.5 months for Asians compared with 9.6 months for whites regardless of whether they received Erbitux. In fact, Asians appeared to do worse with the addition of Erbitux: Overall survival for Asian patients who received Erbitux was 17.6 months compared with 20.4 months for Asians on chemotherapy alone. Whites, on the other hand, lived a median of about a month longer if they received Erbitux plus chemotherapy (10.5 months compared with 9.1 months).

"I think this helps to illustrate ... some of the things that we've seen in the past comparing results from Japanese studies, for example, versus U.S. studies, and seeing differences in outcome," Sandler said. "We may be starting to get some explanation for some of that." More specifically, the data indicated a higher percentage of Asians were female, never-smokers, had a type of NSCLC called adenocarcinoma (as opposed to the more common squamous cell carcinoma), and received other targeted anti-cancer drugs post-study. Because Asians made

up only 10 percent of the roughly 1,100 patients in the study (whites made up about 86 percent), Sandler said the differences did not allow researchers to draw definitive conclusions.

As for the fate of Erbitux in lung cancer, ImClone Systems and Bristol-Myers Squibb, makers of the drug, pulled the FDA application in January, less than two months after submitting it, because of issues related to the drug's formulation. The FLEX trial was conducted outside the U.S., and the formulation supplied by Merck KGaA, ImClone's partner for Erbitux outside North America, was slightly different.

The FDA is allowing the companies to conduct a pre-clinical study to confirm the comparability of the drug manufactured in the U.S. with the one manufactured overseas, a spokesman for BMS said in an e-mail statement. Pending those results, they expect to resubmit the application for approval in NSCLC in the second half of this year.

The question is, according to Sandler, will the FDA approve Erbitux (cetuximab) for use in combination with cisplatin and vinorelbine—the regimen used in the FLEX trial. In the United States, a platinum-based drug (cisplatin or carboplatin) with a taxane, such as Taxol (paclitaxel) or Taxotere (docetaxel), is the most widely used combination for lung cancer treatment.

"I'd like everybody to raise their hand [if] you, in the past year, have utilized cisplatin/vinorelbine in the front-line treatment of metastatic non-small cell lung cancer," Sandler asked the audience. Of the nearly 200 physicians, nurses, and other health care professionals in the room, no hands went up. "That's what I thought. So what's going to happen if it's approved and what is everyone going to do with it? We'll find out."

The Practical Applications of New Agents in Oncology meeting was hosted by the University of Texas Health Science Center at San Antonio's Cancer Therapy and Research Center, well known for its San Antonio Breast Cancer Symposium held each December.