Karen McDonald (Admin Assist to Dr. Denic)

From: Nebojsa Denic
Sent: January 7, 2008 10:43 AM
To: Terry Gulliver
Subject: RE:

Thanks I just read it. Don brought it to my office.

Nebojsa (Nash) Denic, MD,M.Sc., Ph.D. FRCPC
Clinical Chief Laboratory Medicine Program
St. Clare's Hospital, Eastern Health,
154 LeMarchant Road, St. John's, NL, A1C 5B8
T:709-777-5495
F:709-777-5178
E-mail:nebojsa.denic@easternhealth.ca

From: Terry Gulliver
Sent: January 7, 2008 10:42 AM
To: Terry Gulliver; Barry Dyer; Nebojsa Denic
Subject:

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Bad Cancer Tests Drawing Scrutiny

By ANNA WILDE MATHEWS
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Thousands of breast-cancer patients may be getting the wrong treatment because of errors in two laboratory tests widely used to determine which drugs are prescribed.

The tests are used to help determine whether women with invasive breast cancer will receive drugs such as Genentech Inc.'s Herceptin, GlaxoSmithKline PLC's Tykerb and a number of antihormone medications, including the generic tamoxifen and newer treatments such as AstraZeneca PLC's Arimidex and Faslodex.

The pharmaceuticals industry is trying to develop more medicines tailored to the individual characteristics of patients and their diseases. Herceptin, which went on the market in 1998, has been hailed as a breakthrough because it is designed for a certain subset of breast-cancer patients rather than everyone who has the disease.

But recent studies that turned up problems in testing point to a potential snag for such drugs: They depend on accurate lab results.

"We all make the assumption that every test is done well. It turns out it's not a correct assumption," says Lee Newcomer, a cancer doctor who is senior vice president at insurer UnitedHealth Group Inc. Several major private insurers, including UnitedHealth, Aetna Inc. and WellPoint Inc., say they will generally

pay for second-opinion breast-cancer tests. However, Dr. Newcomer says that even though UnitedHealth covers a second test, few doctors order them.

In 2007, around 178,000 patients were expected to be diagnosed with invasive breast cancer in the U.S., according to the American Cancer Society. The tests relating to Herceptin and the antihomone drugs are less straightforward than many traditional lab procedures. They require pathologists to make judgment calls after looking at tissue through a microscope, rather than giving simple yes-or-no answers as in a pregnancy test.

One test examines whether a patient's tumor cells have too much of a protein called Her-2. If they do, Herceptin can help by targeting and destroying those cells. The other test checks for the presence of cell proteins that serve as receptors for the hormones estrogen or progesterone. These hormones can help tumors grow, so if the test is positive, doctors often prescribe drugs such as tamoxifen to suppress or block the hormones.

Karen Ivester, a manager at a construction firm in Boca Raton, Fla., was first diagnosed with breast cancer in 2002, when a marble-sized tumor was removed from her right breast. Ms. Ivester, 50 years old, says the local lab found her negative on both tests, meaning she wasn't given Herceptin or hormone therapy. She weathered chemotherapy and radiation.

Last year, after Ms. Ivester had a shooting pain in her ribs during a golf match, doctors found her cancer had returned in the bones of her spine. The new tumor tested positive on the hormone test. More surprisingly, so did her 2002 tumor, which was retested. Her current doctor, Chuck Vogel, says early use of tamoxifen might have headed off or delayed the cancer's return.

"I was absolutely, absolutely furious to know it was wrong, it could have been wrong," Ms. Ivester says. "I lost my first line of defense, and who knows what difference it would have made."

In a study published in 2006 on Her-2 tests -- led by researchers at Genentech -- a large laboratory that is experienced in the procedures reviewed tests performed by local labs around the country. It found that 14% to 16% of those judged positive for Her-2 were actually negative. Of those judged negative, 18% to 23% were in fact positive.

After signs of problems with hormone testing at a lab in Newfoundland, tissue from 763 patients with negative results was retested at a different lab in 2005 and 2006. The new tests concluded that 317 of those were actually positive. Officials at the provincial Eastern Regional Health Authority in Newfoundland, which oversees the lab that had inaccurate tests, said they can't comment on potential causes for the problems because of an ongoing government inquiry and a class-action suit by patients. But they said the authority did pursue the issue.

In another analysis of labs in multiple countries, published online last August in the Journal of Clinical Oncology, 70% of 105 patients scored as negative on the estrogen test were relabeled as positive when the tissue was retested by an experienced lab. The analysis found that positive results were almost always correct.

"If we tried to market pregnancy tests with this rate of inaccuracy, they would be taken off the market," says Allen Gown, chief pathologist of PhenoPath Laboratories, a Seattle lab. "It means there are a lot of women being treated inappropriately." When PhenoPath checked its performance on both breast-cancer tests using different methods, its results were consistent at least 95% of the time, he said.

In the U.S., such concerns could add momentum to efforts by Congress and consumer groups to push for increased oversight over the lab-testing business, which is booming because of factors such as the rise in genetic testing and the aging of the Baby Boom generation. In 2007, overall lab revenues grew 6.5% to around $51.7 billion, according to Washington G-2 Reports, a unit of the Bureau of National Affairs Inc.

"We're going to be looking at a future where diagnostic medicine will be the norm," says Pamela Klein, a vice president at Genentech. She says lab-testing consistency "can still be improved."

While every prescription drug must receive Food and Drug Administration approval, labs have considerable freedom to develop and perform their own tests. The FDA does approve certain testing kits, but labs can tweak the procedures without being required to get a regulatory sign-off on each home-grown method.

Lab-industry officials say this flexibility allows them to quickly translate emerging science into help for patients. They also say labs, which must be inspected every two years by outside examiners, receive strong oversight. "The process and the authority is there and it does work," says Alan Mertz, president of the American Clinical Laboratory Association, a trade group.

"Our system across the industry is a good one, and getting better," said Mara Aspinall, president of the genetics unit at Genzyme Corp., adding she is "very confident" of her own labs' tests.

However, Rolf Ehrnstrom, corporate vice president of research and development at Dako Denmark A/S, a maker of diagnostic tests and equipment manufacturer that sells both Her-2 and hormone-receptor test kits, said that if labs follow the recommendations in testing kits, "you have a much more standardized way of doing it," and the company believes "we need to standardize and make more quality-assurance throughout the labs."

Barry M. Straube, chief medical officer at the U.S. agency that regulates labs, the Centers for Medicare and Medicaid Services, says his agency is examining tougher quality-control requirements. Now labs must pass outside proficiency checks on only 83 types of tests. That list, devised in 1992, doesn't include the breast-cancer tests or dozens of others developed more recently.

"We're considering adding additional tests," Dr. Straube said. The two breast-cancer ones are likely candidates, he says. However, he says that, in general, "oversight is good."

Starting this year, the College of American Pathologists plans to require proficiency checks from the labs it oversees if they want to offer the Her-2 test. The college and the American Society of Clinical Oncology, which issued guidelines for the Her-2 test a year ago, estimated that around 20% of Her-2 testing may be inaccurate.The two groups also plan to look at the other breast-cancer test.

Some industry executives reject the notion that tests are often inaccurate. Joseph Purvis, executive director of clinical research oncology at drug maker AstraZeneca, says he hasn't seen evidence of extensive problems with hormone tests. "I don't think most patients should worry about the quality," he says.

But pathologists and cancer doctors say labs inexperienced in a particular test may not always understand how small variations in procedure can affect results. Reviews of hormone-receptor tests show that findings can change depending on how much the tissue samples are heated and what preservative is used.

Pathologists at Intermountain Healthcare, a hospital group based in Salt Lake City, found that results varied based on the day of the week a patient had surgery -- apparently because tissue that sat in a refrigerator or in preservative over the weekend was different from tissue examined quickly. Intermountain has since changed its procedures.

Hormone-testing methods are "a chaos," says Soonmyung Paik, director of the pathology division at the National Surgical Adjuvant Breast and Bowel Project, a nonprofit clinical research group, because "every lab uses a different method and different criteria to call a case positive."

Write to Anna Wilde Mathews at anna.mathews@wsj.com

Terry Gulliver
Regional Director
Laboratory Medicine Program
777-6373
777-7898 (fax)