## Test Predicts Chemo Benefit in Breast Cancer

## BY BRUCE JANCIN Denver Bureau

SAN ANTONIO — A commercially available genetic test reliably predicts the magnitude of chemotherapy benefit in women with estrogen receptor-positive, lymph node-negative breast cancer, potentially enabling tens of thousands of women per year to safely avoid the toxicity and expense of adjuvant chemotherapy. "This is a major breakthrough for the individualized treatment of patients diagnosed with early breast cancer," Soon-Myoung Paik, M.D., declared at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

The 21-gene test, known as the Oncotype DX, was the subject of two large clinical studies and a favorable cost-benefit analysis presented at the San Antonio breast cancer symposium.

The test, developed and marketed by Genomic Health Inc., previously was shown to predict the likelihood of distant recurrence of tamoxifen-treated node-negative breast cancer.

In a new study, Dr. Paik applied the Oncotype DX to standard, routinely available tumor samples from 651 participants in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-20 trial, in which women with node-negative, estrogen receptor-positive breast cancer were randomized 1:2 to tamoxifen alone or tamoxifen plus chemotherapy.

ADVERSE REACTIONS Resundation is generally well tolerated Adverse reac-tions have usually been mild and transient in clinical studies of 10275 patients. 3.7% were discontinued due to adverse experiences attituitable to resunzatian. The most frequent adverse events thought to be related to resunzatatin were myalgia, consti-pation, asthenia, adominiar jain, and nausea. **Clinical Adverse Experiences**, regardies of caractily assessment, reported in 22% to platelis in Adverse experiences, regardies of caractily assessment, reported in 22% to platelis in the second state of the s placebo-controlled clinical studies of rosuvastatin are shown in Table 1, discontinuations due to adverse events in these studies of up to 12 weeks duration occurred in 3% of patients on rosuvastatin and 5% on placebo

Table 1. Adverse Events in Placebo-Controlled Studies		
	Rosuvastatin	Placebo
dverse event	N=744	N=382
naryngitis	9.0	7.6
eadache	5.5	5.0
arrhea	3.4	2.9
/spepsia	3.4	3.1
ausea	3.4	3.1
yalgia	2.8	1.3
sthenia	2.7	2.6
ack pain	2.6	2.4
u syndrome	2.3	1.8
rinary tract infection	2.3	1.6
hinitis	2.2	2.1
nucitie	2.0	1.8

Hillings 22.2 Simulation. The following adverse events were reported, repartless of acadity assess-in additional to 10:75 patients treads with reparatises of acadity assess-need injury check patients patient with reparatise at a det exclosion. Enformments and injury check patients patient patient at a det exclosion. Enformments of the patient patient patient patient patient and an application. Digestive System: Hypertension, angina pecker, savoditation, and patipation. Digestive System: Constigation, gastropenetric, varioutiation, and patipation. Digestive System: Constigation, gastropenetric, varioutiation, and patipation. Digestive System: Constigation, gastropenetric, varioutiation, and patipation. Digestive System: Arthroise. Datelets mellium hereis of typerpatient System: Romonia and echymonis. Metabalic and Muntitional Disorders: Regineral defma Musculoskiellation. System: Arthroise, monthesis, composition, anxiety, vertigo, and neuralgia. Sin and Agenedages: Rash and puritus. Laboratory Anormaillies: In the resurvestatin recommende dose rango (i.e. Qo N). However, this finding was more frequent in patients taking rossivastatin 40 mg, when compared to lower doses of resurvestation of unsurvestatin theorem is not associated with wors-omparator stating, though it was generally transitic and was not associated with wors-sing and the singe in the singe the singer through transition. comparator statins, though it was generally transient and was not associated with wors-ening renal function. (See PRECAUTIONS, Laboratory Tests.) Other abnormal laboratory ening treat indicator. (See Precised 1005, calculation) resists, Joine adamtoria tabidatory values reported were elevaled creatinine phospholinas, Enanimases, hyperglycemia, glutany transpeptidesa, alkaline phosphatase, ilihiubin, and thyroid function abnormal-ties. Other adverse vents reported less frequently than 1% in the rossvastatin clinical study rogram, regardless of causality assessment, included antythmia, hepatitis, hypersensitivity reactions (e.e., face defamilia, thormolocypoine), leukopenia, vesiculobu-lous rash, urticaria, and anjuedema), ködney fallure. syncope, mysthemia, myssilis, pancrealitis, photosensitivity reaction, myogath, and rhadbadmoryJosis.

of overdose, the patient should be treated symptomatically and supportive measures instituted as required. Hemodialysis does not significantly enhance clearance of

Internetation repeate the control of the second sec Sing once tash may be denoted by patients relationing tess algorithm. It is not what have predisposing tasks to removable (see WANNINGS, Moyadaw) Rhatdomyolysis). For patients with marked hypercholestoroismic (LDL < 1.98 mg/L) and aggressive injudications, a second statistic dose may be considered. The 40 mg dose of CRESTOR should be reserved for those patients with bare not achieved upon tite-tion of CRESTOR, high levels should be analyzed within 2 to 4 weeks and dospared high LDL < 4 2 mg (ase WANNINGS, Mypogality/Mandomyolysis). Alter mitation and/er upon tite-tion of CRESTOR, high levels should be analyzed within 2 to 4 weeks and dospared higher the maximum recommended day locate should be analyzed within 2 to 4 weeks and dospared higher patients as an adjunct to other high-downing treatments (e.g., LDL aphreness) or if such that the maximum recommended day locate should be analyzed within 2 to 4 weeks and dospared higher patients as an adjunct to other high-downing treatments (e.g., LDL aphreness) or if such LDL C in the Conseque in Potients 1 MG/CISTOR in 30 more day (e.g. WANNINGS, Wyperkensitement and the Underlowering treatments (e.g., LDL aphreness) or if such the constraints and the underlowering treatments (e.g., LDL aphreness) or if such the constraints and the underlowering treatments (e.g., LDL aphreness) or if such the constraints and the underlowering treatments (e.g., LDL aphreness) or if such the constraints and the underlowering treatments (e.g., LDL aphreness) or if such the constraints and the constraints on the label and binding end (e.g. WANNINGS, Wyperkensite, WANNINGS, Wyperkensity/Windowering/Weish and add (e.g. WANNINGS, Wyperkensity/Windowering/Weish and add (e.g. WANNINGS, Wyperkensity/Windowering/Weish theration of the assessity for patients with mit the moderate real insofitiency. If matients and add (e.g. WANNINGS, Wyperkensity/Windowering/Weish and add (e.g. WANNINGS, Wyperkensity/Windowering/Weish and add (e.g. WANNINGS, Wyperkensity/Windowering/Wei cation of dosage is necessary for patients with mild to moderate real insufficiency (Mo modifi-patients with severe renal impairment (( $c_{eq} > 30 m. minn T, 27 m)$  not on hemotiaples, dosing of CRESTOR should be started at 5 mg once daily and not to exceed 10 mg once daily (see FRECAUTIONS, General, and CLINICAL PHARMACOLOGY, Special Populations, Renal Insufficiency).

References: 1. Data on file. DA-CRS-13. 2. Shepherd J, Hunninghake DB, Stein EA, et al Heterenexts: I. Juara on Ime, DA-USA-1.3. Singiplero J., Huminighake DS, Johim PA, et al. The safety of rosuvastatin. Am J Cardiol. 2004;94:882-888. 3. Prescribing Information for CRESTOR. NatraZeneca. Wilminighton, DE. 4. Rosuvastatin Information Web site. Rosuvastatin Clinical Information-Postmarketing Experience, Safety Information. Available at: http://www.rsuvastaininformation.com. Accessed November 90, 2004 5. IIIS National rescription Audit November 2003-600-ber 2004. 6 Groundy SM Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the Nationa Cholesterol Education Program Adut Treatment Panel III guidelines. *Circulation* Colocitical - 2003-0, Alones PH, Davidson MH, Shite FLA, et al. Comparison on the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin and oses (STELLAR trial). Am J Cardiol. 2003;93:152-160. 8. Data on file, DA-CRS-01

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The rationale for applying the tumor gene-expression assay to this patient population lies in the fact that current guidelines recommend adjuvant chemotherapy in the great majority of such patients, yet prior studies demonstrate the clinical benefit is concentrated in only about 15% of the treated population. That means roughly 85% of early-stage breast cancer patients are being overtreated with chemotherapy, explained Dr. Paik, director of the division of pathology at the NSABP in Pittsburgh.

A total of 25% of participants in the B-20 trial had a high recurrence score on the Oncotype DX, meaning at least 31 out of a possible 100 points. Women in this group experienced a dramatic benefit from ad-



This is a maior breakthrough for the individualized treatment of patients with early breast cancer.

DR. PAIK

juvant chemotherapy. Their 10-year distant recurrence-free survival rate was 88% with chemotherapy and 60% without it.

A total of 54% of B-20 participants had an Oncotype DX score below 18, defining them as low risk. They derived essentially no benefit from chemotherapy

Dr. Paik's study was supported by the National Cancer Institute, as well as Genomic Health. He is coholder of a patent for the polymerase chain reaction (PCR) assay used in the study.

'These data advance the state of the art in cancer care and call for a reevaluation of treatment practice. By using the Oncotype DX assay, physicians can more effectively optimize a treatment plan and avoid undertreating and overtreating breast cancer patients," commented NSABP Chair Norman Wolmark, M.D., who is also chair of the department of human oncology at Allegheny General Hospital, Pittsburgh.

In a separate presentation, Laurel A. Habel, Ph.D., reported on a large populationbased, case-control study involving patients with node-negative, estrogen receptor-positive early breast cancer treated at 14 Northern California Kaiser Permanente hospitals. The study population consisted of 220 women who had died of their disease and 570 matched controls who had not.

Tamoxifen-treated patients with a low recurrence score on the Oncotype DX test had a 2.8% mortality rate at 10 years, compared with 10.7% in those with an intermediate score of 18-30 and 15.5% in women with a high score.

In a multivariate analysis, recurrence score on the Oncotype DX test was by far the strongest independent predictor of 10year breast cancer death, with an odds ratio of 6.5. In contrast, a tumor grade of moderate as compared with well-differentiated was associated with an odds ratio of 2.3. Another standard prognostic factortumor size-had an odds ratio of just 1.7, noted Dr. Habel of the Kaiser Permanente division of research, Oakland, Calif.

Continued on following page

BRIEF SUMMARY: For full Prescribing Information, see package insert. INDICATIONS AND USAGE CRESTOR is indicated: 1 as an adjunct to diet to fucture eakerds totabe. CILC-L, Rods monthUL- and Tolevais and to increase HU-C in patients with primary hypercholasterolemic (heterozypus familial and nordamilia) and mixed dyslipidemia (Fredrickson Type III and IIb); 2, as an adjunct to diet for the treat-ment of patients with elevated serum TG levels (Fredrickson Lype IV). 3 to reduce LDL-c, tota-4, and ApOI in patients with homozypus familial hypercholesterolema as a diquinct to dire High-doweding treatments are elevated and the treatments are

unavailable. CONTRAINDICATIONS CRESTOR is contraindicated in patients with a known hypersensitivity to any component of this product. Resurvatatin is contraindicated in patients with arbit liver disease or with unexplained persistent elevations of serum transmisses (see WARININGS, Liver Erzymes). Pregnancy and Lactotion Alternesstensis is a chronic process and discontinuation of light-lowering drugs during pregnarcy should have little impact on the undown of long-term theragy of primary hypercholestorolemia. Cholesterol and other products of cholesterol biosynthesis and essential components for feld diredopment (including symhesis of steriots and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, plossoly use symiless to their unougcay acress suscainces between their choicestery they may cause leta harm when administered to pregrant women. Therefore, MM-GOA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. ROSUVASTAIN SHOULD BE ADMINISTERED TO WOMENO FOLIDEARING AGE ONLY WHEN SUCH PATIENTS ARE HIGHLY UNLIKELY TO CONCEVE AND HAVE BEEN NORMED OF TPOETINTH. HARGEN I the platent becomes pregnant while taking this drug, therapy should be discontinued immediately and the patient apprised of the the fetu

WARNINGS Liver Enzymes HMG-CoA reductase inhibitors, like some other WARNINGS liver Enzymes iMIc-GoA reductase inhibitors, like some other lipid-overing thereines, have been associated with holdennicia abnormatilies of liver function. The incidence of persistent elevations (>3 times the upper limit of normal (ULN) occurring on 2 or more consecutive occasions i) neurun transaminases in fixed does studies was 0.4 o.0 and 0.1% in partients who received resursatint 5, 10, 20, and 40 mg, respectively. In most cases, the elevations were transient and resolved or cases of jaundice, for which a relationship to resursatint for the were two cases of jaundice, for which a relationship to resursatint metragy. There were two cases of lipide after discrimination of theragy. There were no cases of liver failure or investible liver failes and the weet live failure or investible liver dates as in these traits. It is recommended that liver function therage indications that therage individent of theragy. The initiation of therage. tatuite of interversion inter disease in these trans. It is recommended that inter function tests be performed before and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (e.g., semiannually) thereafter. Liver enzyme changes generally occur in the first 3 months of treatment with rosuvastatin. Patients charge generally occur in the first 3 months of treatment with resussation. Patients who develop increased transmissions etcels should be moniced until the admormalities have resolved. Should an increase in ALT or AST of 3 times ULV presist, refuction of does or withdrawal of resussatian is recommended. Resussatian should be used with caution in patients who consume substantial quantifies of alcohol and/or have a history of liver disease (see CLINICLA PHANADOLOGY, Special Populations, Hepatic Insufficiency). Active liver disease or unexplained persistent transminase elevations are contraindications to the use of insuvastatin (see CONTRAINDICATIONS). Myoporthy/Rhob/comyolysis Rare cases of nabdomyolisis with acute renal faulter secondry to myoploinnin have been reported with resussatian i advitt ther drugs in this class. Uncomplicated myligin tas been reported with resussatian with other drugs in this class. Uncomplicated myligin tas been reported with resussatian advitted patients (see AVDFRSE REARCINDS), Carathine kines (CK) elevations (-) to up to 40 mg) in clinical studies. Transmer-related mycastatin classes of muscle weakness in conjunction with increases in CK values -30 times upper limit of mormal, was reported in up to 1.% of distins thairy consuscitant doeses of up to 40 mg in clinical studies. Transmer-related mycastin scattors due to 10 advittor muscle acades of the mylophomylopis were seen with higher than recom-mended doese 100 mg of consuscitatin (scattors that may prelispose Indinical studies: Tare of the proving the studies and the studies of the toring indinical studies are case of industry physics were seen with higher than recom-mended doese (80 mg) of resourcestatin in clinical this. Faztors that may predispose splerists to myophysic with Mid-CoA reductase inhibitos include advanced age (255 years), https://providiam. and reral instifications, The incidence of myopathy increased at doese of rowardstatin above the recommended doese radio myopathy increased at doese of rowardstatin above on weakness, particularly of a more myopathy, social on the state of the state of the state of the state of the myopathy scale state of the myopathy scale state in the state state of the makes on the state state and metals and myophyrolidism. 2. 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S Resuvestalin therary should also be temporarily withheil in any patient with an acute, serious condition suggestive of myopathy or predispasing to the development of renal failure secondary to habdoomylysis (e.g., specis, hypotension, major surgery, tauma, severe melabolic, endocrine, and electrolyte disorders, or unanthrelia estrumest. ed sei

uncontrolled setures). PRECAUTODS General Before instituting therapy with resuvatatin, an attempt should be made to control hypercholestepelmia with appropriate def and sex-cise, weight reduction in obese patients, and treatment of underlying medical problems (see NIDCATORS NID USAGE). Administration of rossvastatin 20 mg to patients with server rerail impairment (CL<sub>4</sub> <00 mL/min/1.2 m<sup>2</sup>) resulted in a 3-dord increase in lipsma concentrations of rossvastatin compared with healthy volunteers (see WARINGS, Myopathy/Rhaddomyolysis and DOSAGE AND ADMINISTRATION). Harmacokinets cludies show an approximate 2-dold elevation in median exposure in Japanese subjects residing in Japan and in Chinese subjects residing in Singapore compared with Caucasian residing in Inforth America and Europe. The contribution of environmental and genetic factors to the difference observed has not bene determined. environmental and genetic tators to the dimeterio observed has not been determined, however, these increases should be considered when mains prosuvostatin dosing deci-sions for patients of Japanese and Chinese anestry. (See WARNINGS, Myogathy Rabdomyohysis, CLINICL, HYARMAROLOOK, Specific Jacompanied by mailse or planet muscle pain, tendentes, para evalues, parafoundir y Lacompanied by mailse or fever. When taking rossvastatin with an aluminum and magnesium hydroide comhin-tion anticol, the antid should be taken at least 2 hours after increasestatin administration tion attack the attack should be taken at least 2 hours after resourcitatin administization (see CLINICAL PHARMOLOGICK, roug interactions), Laboratory Tests In the rosurcitatin clinical trial program, disckic-positive proteinuria and microscopic hematrix are to selvered amon grosurcitatin-triated patients: predominantly in patients dosed above the recommended dose range (i.e. 80 mg). However, this finding vais more requerit in patients taking rosurcitatin 40 mg, when compared to lower doses of rosurcitatin or comparator statins, though it was apenerally transient and was not associ-ated with worsening renal function. Atthough the dirical splits on rosurcitatin 0 rosurcitation unknown, a dose reduction should be considered for patients on rosurcitation. Drug Interactions Cplitspatnies: When rosurcitatin 10 mg was coastiministered with vocesnic tarbaptant patients, rosurcitatin man Cu<sub>2</sub> and mean ALD were increased 11-fold and 7-fold, respectively, compared with healthy volunteers. These

ncreases are considered to be clinically significant and require special considera the design of insuradatiin to patients taking concomitant cyclosophine (see WARIII) Myopathy/Rhabdomyolysis, and DOSAGE AND ADMINISTRATION). Warfarin: On ministration of insurastatiin to patients on stable warfarin therapy resulted clinically significant rises in IMR ( $\leq$ 4, baseline 23). In patients taking comarin antico utants and rossvastatin concentainally. IMR should be determined before start rosuvastatin and frequently enough during early therapy to ensure that no significant alteration of INR occurs. Once a stable INR time has been documented, INR can be moniabarditor of NR occurs. Once a stable INR time has been documented, INR can be more freed at the intervence scalar with the same procedure should be repeated to end at the intervence scalar scalar scalar scalar scalar scalar scalar constraint intervence scalar scalar scalar scalar scalar scalar scalar between the scalar sc test interest table planting best recommended dos Eleminations interesting planting best planting be



≤30 mgAgdar (systemic exposures s60 times the human exposure a14 M mgIdar) kased on AUC comparisons) following treatment to to one year, d10 or to reveal retinal findings. Carcinogenesis, Mutagenesis, Impairment of 0.00 v80 mgAgdar (systemic resposure 2014 does levels of 2.00 v80 mgAgdar s10 mgAgdar s10 v80 mgAgdar s10 v80 mgAgdar s10 v80 mgAgdar s10 mgAgdar s10 v80 mgAgdar s10 v80 mgAgdar s10 v80 mgAgdar s10 v80 mgAgdar s10 mgAgdar s treated with rosuvastatin at 30 mg/kg/day for one month, spermatidic giant cells were seen. Spermatidic giant cells were observed in monkeys after 6-month treatment at seen. Spermatidic giant cells were observed in monkeys after 6-month treatment at 30 mg/ng/tg/m addition to vacualidant of seminiferus tubulere aphtelium. Exposures in the dog vere 20 times and in the monkey 10 times human exposure at 40 mg/dg/ based on body surface area comparisons. Similar findings have been seen with other drugs in this class. **Pregnoncy Pregnancy Category X** see CONTRAINDICATIONS. Rosuvastati in contraindicated in women who are or mg/bacem pregnant. Safely in pregnant women has not been established. There are no adequate and well-controlled software for the statistication in pregnant women. Rosuvastati in corcess the placema and is found in fetal issue and aminotic fluid at 3% and 20%, respectively, of the maternal share noncentration following a soline 5 mg/kg non grade drea on define drea for the maternal found in fetal issue and aminotic fluid at 3% and 20%, respectively, of the maternal share noncentration following a soline 5 mg/kg non grade drea on define drea for an other share noncentration following a soline 5 mg/kg non grade drea on define for the maternal share noncentration following a soline 5 mg/kg non grade drea drea for an other share noncentration following a soline 5 mg/kg non grade drea drea for soline for share noncentration following a soline 5 mg/kg non grade drea drea for share noncentration following a soline 5 mg/kg non grade drea drea for soline for share noncentration following a soline 5 mg/kg non grade for soline for soline for share the soline following a soline for the soline for soline for the following soline for soline for soline for the soline for the following soline for soline for soline for the following soline for the soline for soline for the following soline for the soline for soline for the following soline for the soline for soline for the following soline following sol Pediatric Use ine sarely and effectiveness in pediatric patients have not been statis-lished, Trastamet appendere with Rossvattain in a pediatric population is limited to 8 patients with homozyous FH. None of these patients in scinal studies with resurcatain, 3.159 (31%) were 65 years and older, and 689 (63%) were 75 years and older. The verail frequency of adverse versits and yose of adverse events and versits and versits above and helow 65 years of age. (See WARNINGS, Myopathy/Rhatdomyolysis.) The efficacy of resurvatiant in the geniatric population (265 years of age) was comparable to the efficacy observed in the non-idelity.

## Continued from previous page

The Kaiser study is important because it replicates the NSABP validation study findings in a real-world community-based population. Nearly one-third of participants in the Kaiser study had tumors of 1 cm or less, as is increasingly the case in the contemporary era of widespread mammographic screening, she added.

The Oncotype DX assay uses reversetranscriptase PCR to measure expression of 16 genes involved in cancer proliferation, cancer invasion, estrogen receptor activity, and HER2, along with five reference genes. At a cost of \$3,460, the test is pricey, although Steven Shak, M.D., chief medical officer at Genomic Health, is quick to add that it's a highly complicated assay requiring 1,000 individual steps. For reasons of quality control, it must for the time being be performed on samples shipped to the company's core laboratory.

Despite the test's high price tag, a costbenefit analysis reported at the meeting by Gary H. Lyman, M.D., concluded that routine use of the assay in early-stage breast cancer patients who are estrogen receptor-positive, node-negative, and tamoxifen-treated is cost-effective.

Taking into account the costs of five commonly used chemotherapy regimens,

the use of empiric chemotherapy in such patients costs an average of \$12,923 per year of life gained, compared with \$5,124 per year of life gained with the use of a strategy of selective chemotherapy guided by the Oncotype DX score. The potential savings through routine use of the 21-gene assay were greatest among patients at least 50 years of age, for whom empiric chemotherapy cost an average of \$28,742 per year of life gained, compared with \$16,108 using a selective strategy of Oncotype DX-guided chemotherapy, according to Dr. Lyman of the University of Rochester (N.Y.).

He added that his figures understate the

test's true value because they don't factor in the quality-of-life issues that further enhance the attractiveness of a test that safely enables many patients to avoid chemotherapy. Patients dread the toxicities of chemotherapy, including nausea and vomiting, hair loss, profound fatigue, and infections. His study was funded by Genomic Health, as was the Kaiser epidemiologic study.

Future projects will include tweaking the 21-gene assay so it can be applied to patients with node-positive breast cancer, and research on the value of chemotherapy in patients with an intermediate score on the Oncotype DX. 

## **Blood** Test **Predicts Breast** Ca Outcome

SAN ANTONIO - An elevated circulating tumor cell count at any point during systemic therapy for metastatic breast cancer indicates a high likelihood of rapid disease progression and mortality from that time on, Daniel F. Hayes, M.D., said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

This implies that circulating tumor cell count, as measured by a commercially available blood test, may have an important role in patient monitoring and treatment. A randomized prospective clinical trial is now underway to evaluate the impact of switching therapy in patients who develop an elevated circulating tumor cell (CTC) count during therapy, added Dr. Hayes, clinical director of the breast cancer program at the University of Michigan Comprehensive Cancer Center, Ann Arbor.

In a previously reported double-blind multicenter study of 177 women who were about to start a new therapy for metastatic breast cancer, Dr. Hayes and his coinvestigators showed that the presence of at least 5 CTCs per 7.5 mL of whole blood using the CellSearch test was associated with significantly reduced progression-free and overall survival.

The same held true for patients with a positive test at their first follow-up visit after treatment initiation. They had a median 2.1-month progression-free survival from that time, compared with 7.0 months in women with 0-4 CTCs on the test. Their median overall survival was 8.2 months, compared with more than 18 months in those with a negative CellSearch test, said Dr. Hayes, a consultant to Immunicon, the company that developed the test.

In a multivariate regression model, CTC count at baseline and first follow-up visit were the strongest predictors of progression-free and overall survival, outperforming HER2/neu status, tumor receptor status, type of therapy, and other standard predictors (N. Engl. J. Med. 2004;351:781-91).

In Dr. Hayes's new analysis of the same patient cohort, he demonstrated that patients who developed an elevated CTC count at the second, third, or fourth follow-up visit also fared significantly worse than those who continued to have fewer than 5 tumor cells at their blood draw. -Bruce Jancin



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