

## Metastatic Breast Cancer Survival Improved

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VANCOUVER, British Columbia, July 23 -- Systemic therapies for metastatic breast cancer introduced over the past decade appear to have improved survival, according to the first population-based study to support this long-suspected benefit.

Women diagnosed with metastatic breast cancer in the late 1990s in British Columbia had about a 30% longer survival time than those diagnosed in the early- to mid-1990s, found Stephen Chia, M.D., of the University of British Columbia, here, and the British Columbia Cancer Agency in Victoria, and colleagues.

The survival benefit -- about 7.5 months -- was linked to introduction of aromatase inhibitors, docetaxel (Taxotere), and trastuzumab (Herceptin), they reported in the Sept. 1 issue of the journal *CANCER*.

"These data appear to support the notion that widespread access to newer therapies that have demonstrated improved survival in highly selected patients on clinical trials, do appear to translate into population-based survival benefits," they wrote.

Although epidemiologic studies have supported a fall in breast cancer mortality in the United States and Britain over the last 15 years and clinical trials have supported a survival benefit for newer systemic therapies for metastatic breast cancer, there had not been a population-based study to confirm the association, the investigators said.

So, they studied databases of the British Columbia Cancer Agency, which is involved with care for about 75% of breast cancer patients in the province.

The researchers linked central pharmacy data with the Agency's Breast Cancer Outcomes Database to monitor survival as a function of time when new treatments became widely available. The cohorts were:

January 1991 through December 1992 as baseline.

January 1994 through December 1995 when paclitaxel and vinorelbine (Navelbine) became available in the province for metastatic breast cancer.

January 1997 through December 1998 when the aromatase inhibitors and docetaxel were approved there for metastatic breast cancer.

July 1999 through June 2001 when trastuzumab and capecitabine (Xeloda) became widely available in the province for metastatic breast cancer.

The analysis included 2,150 women in the databases who were age 75 or younger at diagnosis of metastatic breast cancer.

The proportion who had distant metastasis as their initial breast cancer diagnosis was 27% of the 423 patients in the baseline cohort, 18% of the 561 patients in the second cohort, 20% of the 641 in the third cohort, and 22% of the 525 in the most recent cohort.

The proportion of patients who developed distant metastasis within five years of primary breast cancer diagnosis was 70%, 68%, 57%, and 50%, respectively.

Groups were similar in demographic, tumor, and treatment characteristics, except that more women in the later cohorts had estrogen receptor (ER) positive status ( $P=0.01$ ), received any form of adjuvant chemotherapy ( $P<0.001$ ), had a longer interval from diagnosis to distant recurrence ( $P<0.001$ ), and presented with de novo metastases ( $P=0.004$ ).

At analysis, 93%, 93%, 83%, and 58% of patients had died, respectively, reflecting a significant improvement in median survival over time (436, 450, 564, and 661 days, respectively).

One-year survival rates were 55%, 55%, 64%, and 71%, respectively.

Overall survival was significantly longer for the 1997-'98 cohort than the two earlier cohorts ( $P=0.002$ ) and further improved for the 1999-2001 cohort over the 1997-'98 group ( $P=0.05$ ).

In a multivariate analysis, time of diagnosis was an independent predictor of survival. The two later groups showed significantly improved outcome (hazards ratio 0.84 for 1997 through 1998,  $P=0.011$ , and 0.72 for 1999 through 2001,  $P<0.001$ ) whereas the 1994 through 1995 cohort did not (HR 0.97,  $P=0.65$ ).

Dr. Chia and colleagues noted that this improvement occurred despite an increase in the number of women in the later cohorts who had been previously exposed to chemotherapy in the adjuvant setting, which would tend to decrease the effectiveness of systemic chemotherapy in the metastatic setting.

However, they cautioned, the temporal associations in the study could not conclusively be attributed to a single therapeutic agent or regimen, although they said that "there were differences in the use of newer agents/regimens over time, and these differences appear to be associated with improved survival."

The unequal duration of follow-up between cohorts probably did not bias the study because results were not altered in analyses limited to patients who presented with de novo distant metastases or developed distant recurrence within five years of initial diagnosis.

"Although metastatic breast cancer still is an incurable disease, this study provides optimism for those women who are diagnosed with metastatic breast cancer today," the researchers concluded, "and should provide enthusiasm and evidence that continued research to discover better therapies may translate into further improvements in outcome in the future."

## Action Points

Explain to interested patients that this study supports a survival benefit of systemic chemotherapeutic and hormonal therapies for metastatic breast cancer.

Caution patients that the study could not prove a direct link between any single metastatic breast cancer therapy or regimen and improved survival.

The study was funded through the British Columbia Breast Cancer Outcomes Unit. Dr. Chia reported conflicts of interest for Sanofi Aventis, Hoffmann LaRoche, Astra Zeneca, Novartis, Pfizer, Amgen, Ortho Biotech, and Eli Lilly. Other researchers on the study reported conflicts of interest for the same companies plus Genentech.

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Chia SK, et al "The Impact of New Chemotherapeutic and Hormone Agents on Survival in a Population-based Cohort of Women with Metastatic Breast Cancer" *Cancer* 2007;110.