[News * Analysis * Commentary * Controversy]

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White Paper Predicts: With Continued, Specific Efforts, Cancer Can Become Chronic & Manageable by 2022

BY PEGGY EASTMAN

That was the conclusion of the document by representatives from AACR, the Personalized Medicine Coalition, and Feinstein Kean Healthcare, distributed at this conference. Read what John Mendelsohn, Siddartha Mukherjee, Laura Esserman, and others had to say.

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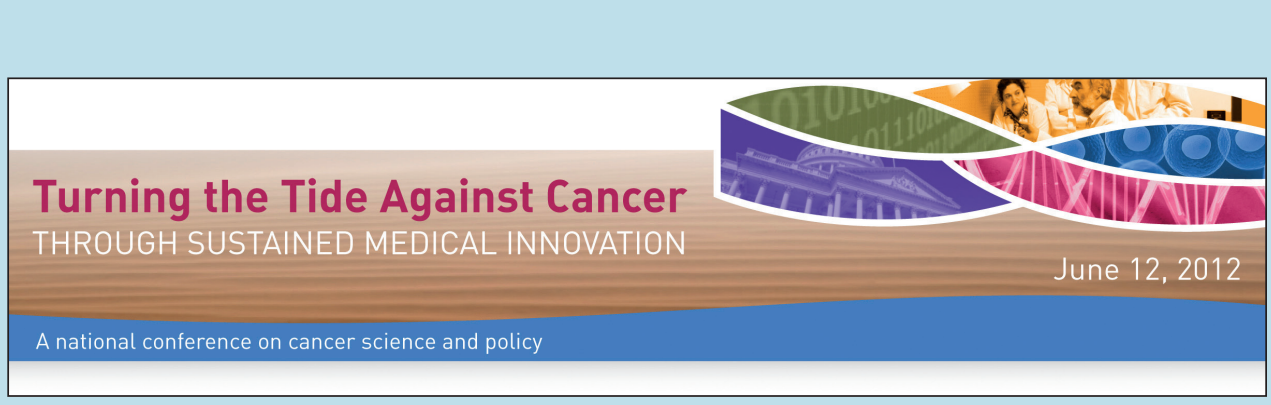
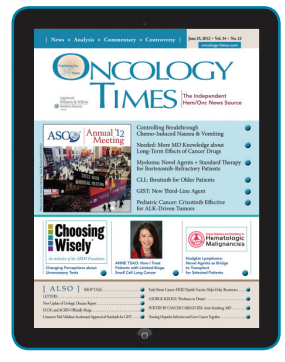


Key Takeaways!

ASCO Annual '12 Meeting

- Personal Picks—ASCO President SANDRA SWAIN
- Hematologic (ALL, CML, CLL, Plasma Cell Dyscrasias)—RAVI VIJ
- GU–WALTER STADLER
- Lung Cancer – RENALDO MARTINS
- Plus: JOE SIMONE on ASCO Past, Present, & Future

Starting on p. 7



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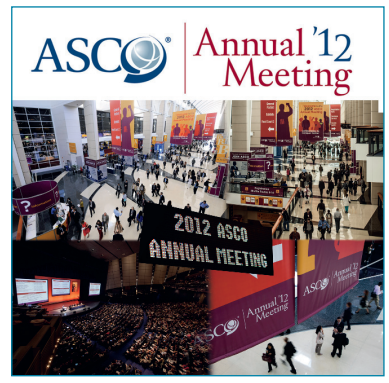
[ALSO]

PERIODICALS

Metastatic Breast Cancer: T-DM1 Conjugate Superior to Standard Treatment with Capecitabine-Lapatinib

BY ROBERT H. CARLSON



"The immunoconjugate, T-DM1, is in a sense a smart bomb, a way to deliver cytotoxic chemotherapy where you want it to be, and largely, but not completely, avoid post-toxicity."

CHICAGO—Trastuzumab has again proved its versatility in breast cancer, this time in combination with the powerful cytotoxic emtansine (T-DM1) to treat women with HER2-positive locally advanced or metastatic breast cancer previously treated with trastuzumab and a taxane.

As presented here at the plenary session of the ASCO Annual Meeting (***Abstract LBA1***), primary results from the Phase III EMILIA trial showed that the antibody-drug conjugate of T-DM1 was superior to the standard capecitabine-lapatinib regimen in both progression-free survival (PFS)—a hazard ratio of 0.650—and overall survival, with a hazard ration of 0.621 at 24 months.

Lead author Kimberly L. Blackwell, MD, Director of the Breast Cancer Clinical Program and Professor of Medicine at Duke Cancer Institute, reported an absolute improvement in median PFS of 3.2 months with T-DM1, and an absolute improvement in overall survival of 17.9 percent.

She explained that emtansine has been shown to be 25 to 500 times more potent than paclitaxel in in-vitro assays, and the combination—T-DM1—incorporates the antitumor activities of trastuzumab and the HER2-targeted delivery of DM1.

Capecitabine-lapatinib is currently the only approved combination for trastuzumab-refractory HER-2-positive metastatic breast cancer.

"T-DM1 is a brand new way of treating breast cancer, and I think it is the first of many antibody-drug conjugates to follow that will link a potent anticancer agent to a targeted delivery system of an antibody," she said.

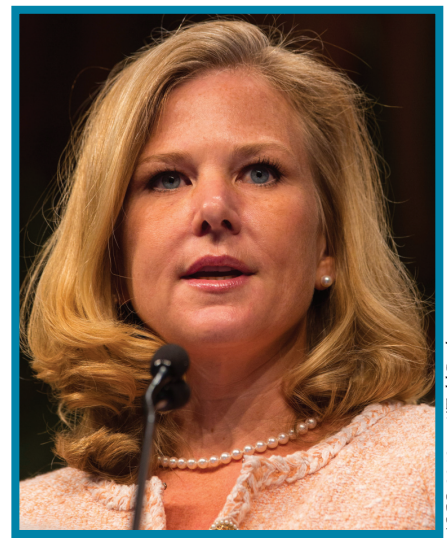
213 Sites in 26 Countries

EMILIA was conducted in 213 sites in 26 countries. Patients received T-DM1 at 3.6 mg/kg IV every three weeks, or oral capecitabine at 1000 mg/m^2 twice daily on days 1-14 every three weeks plus oral lapatinib at 1,250 mg daily. Either regimen was continued until progressive disease or unmanageable toxicity.

A total of 991 patients were enrolled and 978 received treatment. All patients with metastatic disease had received a prior taxane and trastuzumab.

The median duration of follow-up was 12.9 months for patients receiving T-DM1 and 12.4 months for capecitabine-lapatinib.

The overall survival rate was 47.5 percent at 24 months for patients receiving capecitabine-lapatinib versus 65.4 percent for those receiving T-DM1, a 17.9% absolute difference.



ASCO 2012 amit/Todd Buchanan

KIMBERLY L. BLACKWELL, MD: "T-DM1 is a brand new way of treating breast cancer, and I think it is the first of many antibody-drug conjugates to follow that will link a potent anticancer agent to a targeted delivery system of an antibody."

Median progression-free survival was 6.4 months for capecitabine-lapatinib with 304 death events, vs. 9.6 months and 265 events for T-DM1, an absolute improvement in median PFS of 3.2 months.

"Targeted therapy for cancer has progressed another step forward with the EMILIA study."

And median overall survival at interim analysis was 23.3 months for capecitabine-lapatinib with 129 events. There were 94 events with T-DM1 but median survival has not yet been reached.

Safety

Safety also favored T-DM1 including time to symptom progression and other patient-reported outcomes.

There were significantly fewer treatment-related adverse events with T-DM1, Blackwell said, including a 40.8 percent rate of grade 3 or higher adverse events with T-DM1 vs. 57.0 percent for capecitabine-lapatinib.

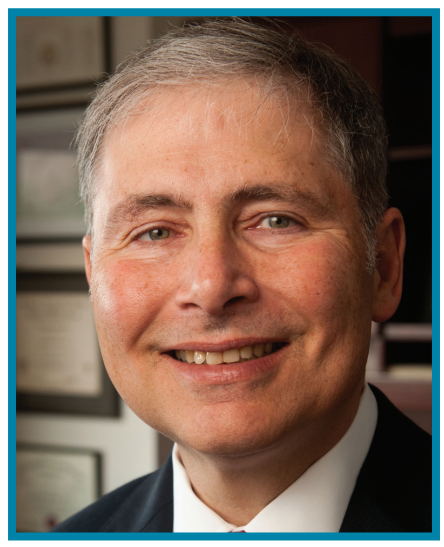
The most common adverse events of grade 3 or higher for T-DM1 were thrombocytopenia (12.9% vs. 0.2% for capecitabine-lapatinib) and increased aspartate aminotransferase (AST) (4.3% vs. 0.8%, respectively).

The most common adverse events of grade 3 or higher for capecitabine-lapatinib were diarrhea (20.7% vs. 1.6% for T-DM1); hand-foot syndrome (16.4% vs. 0% respectively); and vomiting (4.5% vs. 0.8%).

In her conclusion, Blackwell noted that it has been 14 years since trastuzumab was introduced at the 1998 annual ASCO meeting. "Today, the same antibody has been improved in a way that we expect to benefit patients and lessen the toxicity of traditional chemotherapy through use of an antibody-drug conjugate," she said. "Targeted therapy for cancer has progressed another step forward with the EMILIA study."

Discussant: 'Important New Weapon'

"T-DM1 is an important new weapon in the therapeutic armamentarium for breast cancer," said the Discussant for the study, Louis M. Weiner, MD, Director of Georgetown-Lombardi Comprehensive Cancer Center.



LOUIS M. WEINER, MD: "The improved survival is particularly notable, since effective palliative treatment of metastatic breast cancer has rarely been associated with substantially improved survival in the refractory setting. The results of this trial suggest that median survival will be significantly prolonged in women treated with T-DM1."

He congratulated the EMILIA investigators for designing, implementing, and analyzing a Phase III trial that convincingly demonstrated the superiority of T-DM1 therapy compared with a standard regimen.

"Stated simply, T-DM1 really works in this patient population," he said. "The improved survival is particularly notable,

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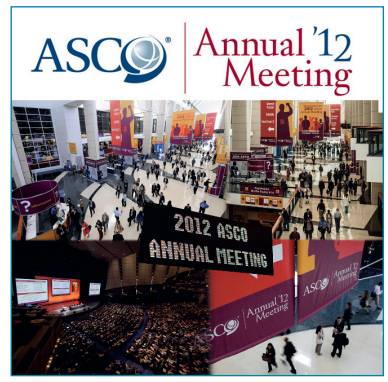
Platinum-Resistant Ovarian Cancer: Bevacizumab Extends PFS

But, Says Discussant: Stop Phase III Trials of Molecularly Targeted Agents in Ovarian Cancer!

BY ROBERT H. CARLSON



CHICAGO—For patients with platinum-resistant recurrent ovarian cancer, a combination of bevacizumab and standard-of-care chemotherapy cuts the risk of disease progression almost in half compared with chemotherapy alone. This and other outcomes from the randomized Phase III AURELIA trial from France were described here at the American Society of Clinical Oncology Annual Meeting (***Abstract LBA5002***).

But in a provocative turn, the Discussant for the study recommended stopping Phase III trials of molecularly targeted agents in ovarian cancer because there are no large groups of homogeneously genomically defined patients with serous cancer, and because there is no strong predictive biomarker in epithelial ovarian cancer.

New Standard Option

"Bevacizumab combined with chemotherapy should be considered a new standard option in platinum-resistant ovarian cancer," said Eric Pujade-Lauraine, MD, PhD, who presented the data on behalf of the AURELIA investigators and the Group d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO).

He said the results are very significant because the addition of bevacizumab offers a new treatment option for the 20 percent of women who have primary platinum-resistant disease, as well as those whose disease later becomes platinum resistant.

Pujade-Lauraine, Professor of Medicine at Université Paris Descartes, said AURELIA is the first randomized Phase III trial in platinum-resistant ovarian cancer to demonstrate benefit with biologic therapy and benefit with a combination regimen vs. monotherapy.

He noted that bevacizumab efficacy with platinum in front-line therapy has already been demonstrated in the Gynecologic Oncology Group 0218 and

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→EMILIA

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since effective palliative treatment of metastatic breast cancer has rarely been associated with substantially improved survival in the refractory setting. The results of this trial suggest that median survival will be significantly prolonged in women treated with T-DM1."

He said more work will be needed to determine if the benefits of T-DM1-based therapy are restricted to patients with HER-2 gene amplification, or if patients with lesser degrees of HER-2 overexpression can be effectively treated as well.

"The utility of T-DM1 in trastuzumab-resistant disease raises obvious questions about the ultimate role of trastuzumab that justify thoughtful clinical investigations that are underway," he concluded.

Trastuzumab has again proved its versatility in breast cancer, this time in combination with the powerful cytotoxic emtansine to treat women with HER2-positive locally advanced or metastatic breast cancer previously treated with trastuzumab and a taxane.

'New Type of Precision Medicine'

Asked for a comment about the study, Andrew Seidman, MD, a breast cancer researcher and attending physician at Memorial Sloan-Kettering Cancer Center, called the results "welcome news."

Seidman, also Professor of Medicine at Weill-Cornell Medical College, said Blackwell's overview of the EMILIA trial highlights one of the most important studies in breast cancer at this meeting—"a new type of precision medicine for breast cancer that is using an old friend, trastuzumab, as a delivery vehicle for a potent cytotoxic agent."

"The immunoconjugate, T-DM1, is in a sense a smart bomb," he said. "It's a way to deliver cytotoxic chemotherapy where you want it to be, and largely, but not completely, avoid post-toxicity."

Speaking of his own experience with T-DM1 at Memorial Sloan-Kettering Cancer Center, ANDREW SEIDMAN, MD, said, "It is kind and gentle. This is not your grandmother's chemotherapy."

He said it is very gratifying to see that this drug outperformed two oral agents given in combination, capecitabine and lapatinib, a standard treatment. "When I say outperformed, it controlled breast cancer for a longer period of time. At first glance, this will likely translate to an overall survival advantage with longer follow-up."

Seidman said he has personal experience with T-DM1 in clinical trials at Memorial Sloan-Kettering: "It is kind and gentle. This is not your grandmother's chemotherapy."

He said he has heard that T-DM1 may be approved by the FDA sometime in 2012.

Also Important: Pertuzumab

Seidman added that it is important to look at a study about pertuzumab, another HER2-targeted agent also developed by Genentech and Roche—the MARIANNE trial of T-DMI and pertuzumab (***clinicaltrials.gov/ct2/show/NCT01120184***).

"The MARIANNE Phase III trial results are awaited to define a possible role for the combination of T-DM1 and pertuzumab as first-line combination therapy of HER2 metastatic breast cancer, " he said.

"Pertuzumab may actually enter our clinics and be used commercially even before TDM-1. So in a sense we have an 'embarrassment of riches' right now for HER-2-positive breast cancers."

He noted that researchers are refining targeted therapy by finding new targets and developing new molecules to hit those targets, by better profiling patients with gene signatures, and finding combination therapies for dual inhibition—"We're also finding that cancer cells, as they have been for many years, are often smarter than the doctors who treat them."

'Old Friend'

Both Dr. Blackwell in her presentation and Dr. Seidman in his interview called trastuzumab "an old friend." In an e-mail exchange, Seidman explained:

"Trastuzumab is indeed an old friend. Since approximately 1999 it has been prolonging survival for women with HER-driven metastatic breast cancer, and doing the same for women with earlier stage disease as adjuvant therapy since 2005. Friends treat us with kindness, and other than uncommon cardiac events, most would agree that it is a kind and gentle agent."