

CONTENTS

Treatment Updates

BY STAFF REPORTS

The annual meetings of the American Society of Hematology and the San Antonio Breast Cancer Symposium were held in December. Each gathering brought together thousands of cancer researchers, physicians, and others to report on critical issues in blood cancers and breast cancer, respectively. Find details at www.fwww.hematology.org and www.sabcs.org. Hematology patients can find additional information on ASH's new patient website, Blood: The Vital Connection (www.bloodthevitalconnection.org). To read *CURE*'s complete coverage from SABCS, visit media.curetoday.com/htmlmail/sabcs/.

AMERICAN SOCIETY OF HEMATOLOGY

Rituxan Combination Scores a Double Hit in CLL

Late-breaking research presented at this year's meeting showed chronic lymphocytic leukemia patients who progressed on prior therapy responded to a Rituxan (rituximab)-based chemotherapy regimen. The phase III REACH study, the largest CLL trial to date in this patient group, randomized 552 patients to receive Fludara (fludarabine) and Cytosan (cyclophosphamide) (FC) with or without Rituxan. Patients in the Rituxan arm had a nearly double complete response rate of 24.3 percent compared with 13 percent in the chemotherapy-only arm. The overall response rate was 69.9 percent compared with 58 percent. The time patients lived without their disease progressing also improved by 10 months, from 20.6 months in the chemotherapy-only arm to 30.6 months with Rituxan. Side effects were similar in both arms, with neutropenia being the most common.

A similar study, but in newly diagnosed CLL patients, is the first randomized controlled trial to test a Rituxan-chemotherapy combination in untreated CLL patients—more than 800 patients, in fact, which is the largest trial to date in this patient group. At the end of six cycles, researchers saw results similar to the REACH study—the addition of Rituxan nearly doubled the complete response rate compared with patients receiving FC alone (44.5 percent compared with 22.9 percent). Median progression-free survival also improved for patients taking Rituxan versus chemotherapy alone (42.8 months compared with 32.3 months). While researchers noted a higher rate of severe neutropenia in the Rituxan arm (33.7 percent versus 21 percent), the rate of infections and other severe side effects were comparable in both arms.

—*Elizabeth Whittington*

Pralatrexate Improves Response for Peripheral T-Cell Lymphoma

Peripheral T-cell lymphoma, an aggressive type of non-Hodgkin lymphoma, has few treatment options, but a phase II international study shows promise for a new chemotherapy agent. The trial, known as PROPEL, examined whether pralatrexate could induce a response in patients who had progressed on other therapies. The 115 patients enrolled in the trial received six weekly infusions of pralatrexate, in addition to vitamin B12 and folic acid to help reduce mucosal side effects. There was no comparison arm in this study because of the relatively low incidence of peripheral T-cell lymphoma and a lack of standard treatments for this disease.

The study reached its goal of achieving a response to the drug, with 11 patients having a complete response and 18 having a partial response. Another 23 patients had stable disease (no disease progression). Common severe side effects in the trial included mucositis and thrombocytopenia. Allos Therapeutics, maker of the drug, plans to submit pralatrexate for approval in the first half of 2009, according to a press statement.

—EW

New Monoclonal Antibody Sparks Response in Refractory CLL

Arzerra (ofatumumab), an experimental monoclonal antibody that targets the CD20 receptor on cancer cells, may become a new treatment option for CLL patients who progress on other therapies, including Fludara (fludarabine) and Campath (alemtuzumab). About half of the 138 patients in the trial responded to the drug. Median overall survival reached 13.7 months for patients treated with prior Fludara and Campath and 15.4 months for patients with bulky disease in their lymph nodes who were previously treated with Fludara only.

The next step will be to test the drug in combination with other agents, although the antibody has significant activity as a monotherapy (therapy that uses only one drug)—something researchers haven't even seen with the original anti-CD20 drug Rituxan. GlaxoSmithKline expects to file Arzerra for approval in January.

—EW

SAN ANTONIO BREAST CANCER SYMPOSIUM

Aromatase Inhibitors More Effective Than Tamoxifen

On the first day of the meeting, a morning session on adjuvant hormonal therapy offered a repetitive theme: Aromatase inhibitors work better than tamoxifen.

According to new data from the BIG 1-98 trial, five years of the aromatase inhibitor Femara (letrozole) reduced the risk of death by about one-fifth when compared with tamoxifen. Some patients on the tamoxifen arm crossed over to

receive Femara, and the reduced risk of death in these patients was 13 percent compared with patients who only received tamoxifen.

To determine the most effective approach for minimizing the risk of recurrence, the BIG 1-98 trial compared three arms: five years of Femara, two years of Femara followed by three years of tamoxifen, and two years of tamoxifen followed by three years of Femara. There was no evidence that sequential treatments improved disease-free survival compared with Femara alone. However, after two years of initial treatment with Femara, the patients who switched to tamoxifen did as well as patients treated with Femara for the entire study period, indicating that patients can switch to tamoxifen if needed, said investigators.

The TEAM trial asked whether five years of Aromasin (exemestane) or tamoxifen works better as single-agent therapy after surgery. The first analysis of this largest-ever trial of an aromatase inhibitor compared with tamoxifen included data from nearly 10,000 women. The trial found a significant advantage for Aromasin over tamoxifen after three years of follow-up.

—*Beverly A. Caley*

Data Support Tykerb Plus Femara for Metastatic Breast Cancer

The combination of Tykerb (lapatinib) and Femara (letrozole) may offer a first-line oral treatment approach for postmenopausal women with hormone receptor-positive, HER2-positive metastatic disease, according to data from the EGF30008 study.

Of 1,286 postmenopausal women with hormone receptor-positive tumors, 219 were also HER2-positive. In this subgroup, treatment with Femara alone resulted in a median progression-free survival of three months compared with more than eight months for patients treated with Femara plus Tykerb. The combination was well tolerated.

Findings in addition to the main result may have implications for future trials based on evidence that Tykerb plus Femara may benefit patients who relapsed while receiving tamoxifen, said researchers.

—*BAC*

New Agents Effectively Target HER2-Positive Cancers

Herceptin (trastuzumab) and Tykerb (lapatinib), two drugs approved for HER2-positive breast cancer, have greatly improved outcomes for patients, but researchers are now looking for new options to target HER2—a needed approach given that some cancers don't respond, while others may develop resistance to the drugs.

Two phase II studies presented in San Antonio looked at new agents for patients whose tumors progressed on existing HER2-targeted therapies. The first study looked at trastuzumab-DM1, an intravenous antibody-drug conjugate in which the cell-killing agent DM1 is attached to the Herceptin antibody. After a median

follow-up of 19 weeks, 42 of 107 patients with HER2-positive metastatic breast cancer had their tumors shrink by at least half. Final efficacy results will be available next year. Common side effects included mild thrombocytopenia, fatigue, and infection. No cases of severe cardiotoxicity, a side effect associated with Herceptin, were reported.

The second study tested a new oral tyrosine kinase inhibitor called neratinib in metastatic and locally advanced HER2-positive breast cancer. Patients were assigned to one of two arms based on whether they had received prior Herceptin therapy. All patients received a daily oral dose of neratinib. Among patients who had already received Herceptin, 26 percent responded compared with 56 percent of patients who had never taken Herceptin. Progression-free survival—the length of time the cancer did not progress—reached 23 weeks for the prior Herceptin arm and 40 weeks for the arm that had not received Herceptin. Diarrhea was the most common side effect, seen in almost all cases and requiring dose reductions for some patients.

—*Melissa Weber*

Looking for the Optimal Treatment Schedule for Taxanes

While a group of chemotherapy drugs known as taxanes have an established role in breast cancer treatment after surgery, new studies investigating the optimal schedule have produced conflicting results.

The phase III NSABP B-30 trial, which compared three schedules and combinations in women with node-positive breast cancer, found that Adriamycin (doxorubicin)/Cytoxan (cyclophosphamide) for four cycles followed by the taxane Taxotere (docetaxel) for four cycles (known as a sequential schedule) decreased mortality by 14 percent compared with Taxotere/Adriamycin/Cytoxan given concurrently for four cycles, and by 17 percent compared with Adriamycin/Taxotere without Cytoxan. Researchers found that the Adriamycin/Taxotere regimen was as effective as Taxotere/Adriamycin/Cytoxan with regard to overall survival. In terms of disease-free survival, the eight-cycle sequential schedule had an even stronger advantage over the other two regimens.

Another phase III trial, BCIRG 005, compared Adriamycin/Cytoxan for four cycles followed by Taxotere for four cycle with Taxotere/Adriamycin/Cytoxan for six cycles in women with HER2-negative, node-positive, early-stage breast cancer. The two regimens were equally effective with regard to disease-free survival.

Taxotere/Adriamycin/Cytoxan was given for the more conventional six cycles to patients in BCIRG 005, whereas the NSABP B-30 trial used four cycles, so investigators commented that patients on Taxotere/Adriamycin/Cytoxan in NSABP B-30 may have been undertreated, and a direct comparative trial of the conventional six cycles of concurrent therapy versus sequential therapy is ongoing.

—*BAC*