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ASCO Releases First-Ever Guidance on Taking Cancer Family Histories

BY PEGGY EASTMAN

The American Society of Clinical Oncology has issued the first specific recommendations for oncologists on taking a cancer family history for each new cancer patient.

The recommendations, published as a Special Article now available online ahead of print in the *Journal of Clinical Oncology* (***DOI:10.1200/JCO.2013.50.9257***), are designed to help oncologists identify patients with a predisposition to hereditary cancer; refer appropriate patients for genetic testing and counseling; select individualized treatment options for these patients; and personalize their surveillance and survivorship plans.

But, as the new report makes clear, there are a number of specific barriers to thorough cancer family history taking that need to be addressed.

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Best Lung Cancer Papers, 2013

BY RAMASWAMY GOVINDAN, MD

Research in the systemic therapy of lung cancer continues to progress at a good pace, and the past year was no exception. Although some of the following studies are no doubt already familiar to *OT* readers from presentations at national and international meetings, I offer here a brief review of the lung cancer papers published in 2013 expected to be most useful for practicing clinicians.

Frontline Therapy

Activating mutations in the epidermal growth factor receptor tyrosine kinase (EGFR TK) are present in 10 to 15 percent of patients with non-small cell lung cancer (NSCLC). Patients with advanced EGFR-mutant NSCLC have higher response rates and longer progression-free survival with reversible EGFR TK inhibitors (gefitinib or erlotinib) compared with patients treated with platinum-based chemotherapy.

The results of the LUX-Lung 3 trial, a randomized Phase III study comparing afatinib with cisplatin and pemetrexed in patients with EGFR-mutant advanced NSCLC were published this year (***JCO 2013;31:3327-3334***).

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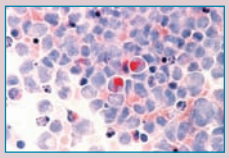
AML: Allogeneic SCT Shown as Option for Older, High-Risk Patients Post-Remission

BY ROBERT H. CARLSON

Data from a prospective matched-pair analysis provide further evidence that allogeneic stem cell transplantation (SCT) from both HLA-identical sibling donors and matched unrelated donors is a viable option for post-remission treatment of patients under age 60 with cytogenetically defined intermediate- or high-risk acute myeloid leukemia (AML).



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AML: ALLOGENEIC SCT FOR OLDER & HIGH-RISK PATIENTS

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The study, now available online ahead of print in the *Journal of Clinical Oncology (**doi 10.1200/JCO.2013.50.5768**)*, compared outcomes of 185 matched pairs identified from the 2,347 patients in the multicenter AMLCG99 trial (***Stelljes M et al: Haematologica 2011;96:972-979***).

> About half of AML patients today are able to find donors, compared with only about one-quarter in the past.

In the new study, patients who underwent allogeneic SCT in first remission were matched to patients who received conventional post-remission therapy. The projected overall seven-year overall survival rate was 58 percent for the allogeneic SCT group versus 46 percent for the conventional post-remission treatment group. Relapse-free survival was 52 percent for SCT and 33 percent in the control group.

"With significantly decreasing rates of transplant-related severe toxicities and mortality, allogeneic stem cell transplant has become a reasonable treatment option even for older patents," said Matthias Stelljes, MD, Senior Attending Physician in the Department of Hematology-Oncology at the University of Muenster, speaking for the German AML Cooperative Group (AMLCG).

"Our data, with relapse rates of around 80 percent in patients over age 45, now support the extension of allogeneic SCT as post-remission therapy especially to these older patients," he said via e-mail.

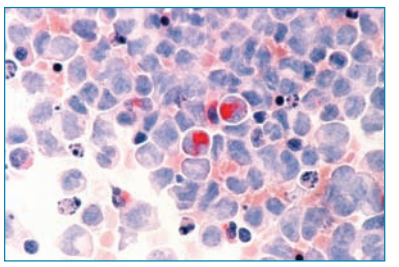
He noted that the study differs from earlier studies that used donor-versus-no-donor comparisons, were restricted to transplants from sibling donors, and showed a benefit of allogeneic SCT mainly for younger AML patients.

MATTHIAS STELLJES, MD, noted that the German AML Cooperative Group has now launched a prospective randomized trial that addresses the impact of allogeneic SCT as post-remission therapy in patients with cytogenetically defined intermediate-risk AML.

In this new trial, overall survival was significantly longer for allogeneic SCT in patient subgroups with nonfavorable chromosomal aberrations, patients older than age 45, and patients with secondary AML or high-risk myelodysplastic syndromes.

Improving Treatment of AML

Asked for his opinion for this article, Steven Devine, MD, Professor of Medicine and Director of the Blood and Marrow Transplant Program at Ohio State University, explained that the trend in the U.S. for intermediate- and adverse-risk patients with AML has been for transplant in first remission.



"The 2011 publication reflected what people were doing anyway, because many groups have made the leap that patients with intermediate- and adverse-risk AML would be referred for transplant, at least if a well-matched sibling or well-matched unrelated donor could be found," he said in a telephone interview. "This matched-pair analysis tried to alleviate a lot of the biases that are inherent in donor-versus-no donor allocation studies. It also demonstrated that patients age 45 to 60 seem to benefit, which had not been shown before."

Devine said clinicians have previously been reluctant to use donors other than matched related siblings, but many different studies over the last decade have shown that the outcomes are quite similar between matched sibling transplants and matched unrelated donor transplants, mainly because of the use of molecular typing.

"The unrelated donors we find are better matches than they were 10 or more years ago."

About half of AML patients today are able to find donors, compared with only about one-quarter in the past, he said. "The field of AML has shifted mainly because of supportive care, HLA typing, and other aspects that affect the risk of treatment-related mortality of allogeneic transplant. Treatment of patients with AML is a moving target—it's always improving."

A decade or more ago, he said, the major reluctance to pursue allogeneic transplantation for intermediate- and adverse-risk patients was due to the risk of non-relapse or treatment-related mortality from the transplant. Patients previously would have received standard or high-dose cytarabine chemotherapy, the same therapy as used in the conventional arm in the Stelljes study, he continued.

STEVEN DEVINE, MD: "The unrelated donors we find are better matches than they were 10 or more years ago."

"Supportive care for acute leukemia patients has probably improved faster than conventional chemotherapy has improved, so the mortality rates have gotten better."

In the future, more than 90 percent of patients might have a donor, Devine said, since the latest studies are suggesting that outcomes for umbilical-cord haploidentical-related transplants are improving. And now it is common for transplant patients with AML who are between ages 60 and 75, based mainly on retrospective and a recently completed prospective nonrandomized study.

Devine said he wondered whether the German researchers would conclude from their data that a well-matched unrelated donor is comparable to a sibling donor. In the U.S., he said, they are considered roughly equivalent.

"Most patients in this study were recipients of matched sibling transplant, so do the researchers consider a matched sibling and a well-matched unrelated donor comparable?" Devine asked. "For a patient with intermediate- or adverse-risk cytogenetics, would the general recommendation be that it makes no difference?"

Stelljes responded by email that the researchers were not able to draw that conclusion from these data. However, he said, a previous study by the AMLCG did show that for high-risk patients, transplants from unrelated or sibling donors can produce comparable results.

Data available today on older patients with AML are not from prospective randomized trials, Stelljes said, and consequently the German AML Cooperative Group has launched a prospective randomized trial that addresses the impact of allogeneic SCT as post-remission therapy in patients with cytogenetically defined intermediate-risk AML (**NCT01246752**).

> "The field of AML has shifted mainly because of supportive care, HLA typing, and other aspects that affect the risk of treatment-related mortality of allogeneic transplant."