Alliance for Clinical Trials in Oncology
NEWS
Summer 2015
Volume 5, No. 3
info@allianceNCTN.org

SPOTLIGHT ON TRIALS

Alliance Study Seeks to Predict Long-term Outcome for Patients with ER+ Breast Cancer

Growth Biomarker Strategy in Neoadjuvant Setting May Provide Answers

Estrogen receptor positive (ER+) breast cancer in postmenopausal women is a major public health problem. In the United States, one in eight women will be diagnosed with breast cancer in their life time.[1] This year, an estimated 234,190 new diagnosis and 40,730 deaths from breast cancer are expected.[2] Among all breast cancer cases, more than 75 percent occur in postmenopausal women, in whom 80 percent of the cases are ER+.[3] Since the majority of breast cancer cases are diagnosed at an early stage (I-III), relapse of early stage disease accounts for the majority of breast cancer deaths.[1] Although ER+ breast cancer tends to recur later in the course of disease than ER- breast cancer, the cumulative rate of recurrence over time is similar for both disease groups.[4,5] Therefore, recurrence of ER+ breast cancer in postmenopausal women is a major contributor of breast cancer mortality.

Adjuvant therapy following curative surgery has significantly improved breast cancer outcome. In the case of ER+ breast cancer, systemic chemotherapy followed by endocrine treatment with tamoxifen has been shown to half the breast cancer mortality rate.[6] The recent introduction of aromatase inhibitors (AIs) in early-stage breast cancer has further reduced the recurrence rate; however, a significant number of patients recur despite the current standard treatment. At a median follow-up of 120 months in patients enrolled in the Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial, recurrence was observed in 19.7 percent and 24.0 percent of patients treated with five years of adjuvant anastrozole and tamoxifen, respectively, with a persistent risk of relapse over time observed in both treatment arms, indicating a need to improve the current standard therapy.[7] However, the evaluation of new agents in the adjuvant setting has traditionally required large number of patients and years of follow up to demonstrate the effectiveness in reducing cancer relapse and/or mortality. The development of surrogate endpoints for disease-free survival (DFS) and overall survival (OS) is needed for efficient drug screening and to expedite the drug development process.

The trial **Alliance A011106 – Alternate approaches for clinical stage II or III estrogen receptor positive breast cancer neoadjuvant treatment (ALTERNATE) in postmenopausal women** may provide a solution. The goal of this trial is to develop a Ki67-based (growth) biomarker strategy in the neoadjuvant setting to predict long-term outcome of patients with ER+ breast cancer. Alliance researchers intend to validate the achievement of the Modified Preoperative Endocrine Prognostic Index (PEPI) score of 0, post neoadjuvant endocrine therapy as a surrogate marker of success for DFS.[8] Based on promising data in the metastatic setting, researchers will also compare fulvestrant alone, fulvestrant in combination with anastrozole, and anastrozole alone in regards to the rate of modified PEPI 0, to provide rationale for future adjuvant studies of fulvestrant in ER+ early stage breast cancer. In this trial, endocrine resistant tumors are identified early by Ki67 assessment on the four-week tumor (required) and then the 12-week (optional) biopsies. Patients with tumor levels of Ki67 greater than 10 percent at these time points will be switched to neoadjuvant weekly paclitaxel, or other standard taxane and/or anthracycline or CMF (cyclophosphamide, methotrexate and fluorouracil) regimens to assess the rate of complete pathologic response (pCR) to chemotherapy as a secondary endpoint. By providing validated surrogate endpoints for endocrine

continued on page 6

Alliance Researchers to Study Use of Taxanes in Rare Thyroid Cancer

While thyroid cancer is the most common endocrine malignancy, anaplastic thyroid cancer (ATC) is extremely rare. This year, the estimated incidence rate for thyroid cancer in the United States is about 62,450 newly diagnosed cases, of which ATC comprises less than 2 percent.[1-3] ATC is an undifferentiated, highly aggressive tumor with a median survival of five months from diagnosis and a one-year survival of no more than 20 percent. Patients with ATC die from distant metastases or locoregional disease that destroys the airway. Median age at diagnosis ranges between 63 and 74 years. ATC affects women more frequently than men.[3] A diagnosis of ATC frequently follows a prior or concurrent diagnosis of well-differentiated thyroid cancer or benign nodular thyroid disease, and synchronous pulmonary metastases may be present in up to 50 percent of patients.[3] If detected early, extensive surgery offers the best chance of cure. Combination chemotherapy and hyper-fractionated radiotherapy (RT) are used with limited success, but several clinical studies using taxanes have shown benefit.[4-7] More effective targeted therapies based on a better understanding of the molecular and signaling pathways that are disrupted in ATC are needed.[8-11]

The molecular pathogenesis of thyroid cancer is beginning to be understood, with recent studies describing distinct gene expression patterns. A progression model from more differentiated papillary and follicular carcinomas to undifferentiated ATC has been suggested.[12] Genomic profiling has been performed to identify genes unique to benign versus malignant lesions, including one study of patients with ATC.[13,14] For ATC, oncogenic mutations and frequencies of mutation have been identified for Ras (20 percent to 60 percent) and B- Raf (up to 20 percent).[14,15]

In thyroid cancer, the peroxisome proliferator-activated receptor (PPAR) – which is a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes – may act as a tumor suppressor gene.[16,17] PPARs play essential roles in the regulation of cellular differentiation, development, and metabolism (carbohydrate, lipid, protein), and tumorigenesis of higher organisms.[18-20] PPAR agonists are known to antagonize anti-apoptotic pathways such as survivin, which may account for synergy between PPAR agonists and taxanes, since taxanes upregulate survivin.[21-23] Since survivin is highly expressed in poorly differentiated cancers including ATC, it is hypothesized that the combination of efatutazone, a PPAR agonist that may antagonize survivin, and paclitaxel may enhance antitumor activity.[24,25]

In the trial **Alliance A091305 – A phase 2 randomized study of efatutazone, an oral PPAR agonist, in combination with paclitaxel versus paclitaxel in patients with advanced anaplastic thyroid cancer**, the primary objective is to determine whether the combination of paclitaxel and efatutazone improves overall survival (OS) compared to paclitaxel alone in patients with advanced anaplastic thyroid cancer. Prior studies have shown that the median OS is generally around four months for paclitaxel alone in this stage IV disease population.[10] It is hoped that the combination of these agents can increase the median OS to at least eight months. In addition, the study will compare the confirmed response rate, duration of response, progression-free survival (PFS), and adverse event rates between the combination of paclitaxel and efatutazone versus paclitaxel alone. As an exploratory translational analysis, the association of biomarkers with clinical outcome data will be compared between the two treatment arms in a correlative study. Maximum accrual for this study is 50 patients.

Refer to the study protocol (Alliance A091305), which can be found on the CTSU menu (ctsu.org) for complete information on patient eligibility, the trial design and treatment plan. The Alliance Study Co-Chairs are Robert C. Smallridge, MD, Mayo Clinic Cancer Center, e-mail: smallridge.robert@mayo.edu and Michael Menefee, MD, Mayo Clinic Cancer Center, e-mail: menefee.michael@mayo.edu.

Source

1. Siegel RL, Miller KD, Jemal A Cancer statistics, 2015. CA Cancer J Clin. 2015;65(1):5-29.
2. Abate E, Smallridge R 2011 Managing anaplastic thyroid cancer. Expert Rev Endocrinol Metab. 6:793-809.
3. Smallridge RC, Abate E 2014 In Press Anaplastic Thyroid Carcinoma: Clinical Aspects. In: Wartofsky L, Van Nostrand D, (eds) Thyroid Cancer: A Comprehensive Guide to Clinical Management. Third Edition ed. Springer.
4. Ain KB, Egorin MJ, DeSimone PA 2000 Treatment of anaplastic thyroid carcinoma with paclitaxel: phase 2 trial using ninety-six-hour infusion. Collaborative anaplastic thyroid cancer health intervention trials (CATCHIT) group. Thyroid. 10:587-594.
5. Bhatia A, Rao A, Ang KK, et al, Anaplastic thyroid cancer: clinical outcomes with conformal radiotherapy. Head Neck 2010;32:829-836.
6. Higashiyama T, Ito Y, Hirokawa M, et al. 2010 Induction chemotherapy with weekly paclitaxel administration for anaplastic thyroid carcinoma. Thyroid. 20:7-14.
7. Troch M, Koperek O, Scheuba C, et al. 2010 High efficacy of concomitant treatment of undifferentiated (anaplastic) thyroid cancer with radiation and docetaxel. J Clin Endocrinol Metab. 95:E54-57.
8. Smallridge RC, Copland JA 2010 Anaplastic thyroid carcinoma: pathogenesis and emerging therapies. Clin Oncol. 22:486-497.
9. Smallridge RC, Marlow LA, Copland JA 2009 Anaplastic thyroid cancer: molecular pathogenesis and emerging therapies. Endocr Relat Cancer. 16:17-44.

continued on page 9

Alliance/ASCO Abstracts from 2015 Annual Meeting

This year, nearly 6,000 abstracts were submitted to the annual meeting of the American Society of Clinical Oncology (ASCO) from 85 countries. ASCO is one of the largest medical gatherings in the United States, drawing more than 34,000 oncology professionals for four and a half days of scientific and educational presentations. The Alliance for Clinical Trials in Oncology had 29 abstracts approved for inclusion, on topics ranging from breast to colon cancers to the genetics of cancer, cancer prevention, lymphoma and more. In addition, eight abstracts were presented by other National Clinical Trials Network (NCTN) groups that included Alliance participation. The meeting was held in Chicago, IL May 29-June 2.

Here is a partial list of Alliance abstracts, with synopses.

Cancer Prevention, Genetics, and Epidemiology

Alcohol consumption and prognosis in patients with stage III colon cancer: A correlative analysis of phase III trial NCCTG N0147 (Alliance)

Phipps AI, Shi Q, Limburg PJ, Nelson GD, Sargent DJ, Sinicrope FA, Chan E, Gill S, Goldberg RM, Kahlenberg MS, Nair S, Shields AF, Newcomb PA, Alberts SR. J Clin Oncol 33, 2015 (suppl; abstr 1508)

Synopsis: The relationship between alcohol and survival after colon cancer (CC) has not been well elucidated. Data from N0147, a phase III randomized adjuvant trial in stage III CC, assessed the association of alcohol consumption with CC outcomes (disease-free survival, time-to-recurrence, and overall survival). Alcohol consumption was not associated with CC outcomes overall, though mild to moderate red wine consumption was suggestively associated with more positive outcomes.

Health Services Research and Quality of Care

Cost of chemotherapy for metastatic colorectal cancer with either bevacizumab or cetuximab: Economic analysis of CALGB/SWOG 80405

Schrag D, Dueck AC, Naughton MJ, Niedzwiecki D, Earle C, Shaw JE, Grothey A, Hochster HS, Blanke CD, Venook AP. J Clin Oncol 33, 2015 (suppl; abstr 6504)

Synopsis: Data from CALGB/SWOG 80405, a phase III trial, were examined to compare the economics of adding either bevacizumab or cetuximab to standard first-line chemotherapy for metastatic colorectal cancer (mCRC). Using cost estimates in 2014 USD, acute care costs were similar in the two arms, but drug costs were higher in the cetuximab arm. Bevacizumab is therefore preferable to cetuximab, from a health economic standpoint, for first-line chemotherapy treatment of patients with KRAS wild type mCRC.

Patient and Survivor Care

Comparison between clinician- and patient-reporting of baseline (BL) and post-BL symptomatic toxicities in cancer cooperative group clinical trials (NCCTG N0591 [Alliance])

Atkinson TM, Satele DV, Sloan JA, Mehedint D, Lafky JM, Basch EM, Dueck AC. J Clin Oncol 33, 2015 (suppl; abstr 9520)

Synopsis: Data were pooled from Alliance trials to compare clinician- and patient-reporting of baseline and post-baseline symptomatic toxicities in cancer cooperative group clinical trials. Clinicians consistently under-reported the prevalence of baseline symptoms compared to patients. Change from patient-reported baseline assessment appears to more closely match clinician-graded adverse events. This method should be considered for future patient-based toxicity assessments in clinical trials as a more accurate appraisal of symptoms attributable to study treatments rather than to pre-existing etiologies.

A comparison of the natural history of oxaliplatin- and paclitaxel-induced neuropathy (NCCTG N08C1, N08CB/Alliance)

Ruddy KJ, Pachman D, Qin R, Seisler DK, Smith EML, Puttabasavaiah S, Novotny PJ, Ta LE, Beutler AS, Wagner-Johnston ND, Staff N, Grothey A, Dakhil SR, Loprinzi CL. J Clin Oncol 33, 2015 (suppl; abstr 9564)

Synopsis: This study examined the similarities and differences of paclitaxel and oxaliplatin neuropathy symptoms using data from N08CB and N08C1. Findings included that the acute neuropathy symptoms from both drugs peaked on day three, with acute symptoms experienced in cycle one predicting occurrence in the subsequent cycles. For chronic neuropathy, both drugs caused a predominantly sensory neuropathy (numbness and tingling much more common than pain). Understanding the similarities and differences between these neuropathy syndromes should provide insight into the underlying pathophysiology and help find preventative treatment approaches.

CALGB 70604 (Alliance): A randomized phase III study of standard dosing vs. longer interval dosing of zoledronic acid in metastatic cancer

Himelstein AL, Qin R, Novotny PJ, Seisler DK, Khatcheressian JL, Roberts JD, Grubbs SS, O'Connor T, Weckstein D, Loprinzi CL, Shapiro CL. J Clin Oncol 33, 2015 (suppl; abstr 9501)

Synopsis: This randomized trial tested whether zoledronic acid (ZA) given every three months would be non-inferior to monthly for 24 months in terms of skeletal-related events (SRE) among patients (breast cancer,

continued on next page

prostate cancer, and multiple myeloma) with bone metastases. The proportions of SRE were 29.5 percent versus 28.6 percent (95 percent CI for margin: -3.3 percent to 5.1 percent, Cochran-Maentel-Hanzel p = 0.79) for monthly and every three months, respectively. Thus, ZA administered every three months is non-inferior to ZA administered monthly for 24 months among patients with breast cancer, prostate cancer, or multiple myeloma.

Venlafaxine to prevent oxaliplatin-induced neuropathy? A pilot randomized placebo-controlled trial

Zimmerman CT, Atherton PJ, Pachman DR, Seisler DK, Wagner-Johnston ND, Dakhil SR, Lafky JM, Qin R, Grothey A, Loprinzi CL. J Clin Oncol 33, 2015 (suppl; abstr e20734)

Synopsis: The purpose of this randomized, placebo-controlled, double-blinded pilot study was to try to obtain data to support conducting a phase III trial to test the use of venlafaxine to prevent oxaliplatin neurotoxicity. Although there was a trend toward benefit for the venlafaxine arm compared to placebo for some measures of neuropathy, these positive trends were outweighed by a lack of any such trends in many of the other measurements examined. Results do not support either the use of venlafaxine for preventing oxaliplatin-induced neuropathy in clinical practice or the initiation of a phase III trial.

Quality of life analysis of NCCTG N0877 (Alliance): Phase II trial of either dasatinib or placebo combined with standard chemoradiotherapy for newly diagnosed glioblastoma multiforme (GBM)

Qin R, Tan AD, Sloan JA, Johnson DR, Lesser GJ, Anderson SK, Laack NN. J Clin Oncol 33, 2015 (suppl; abstr e17715)

Synopsis: Patients newly diagnosed with glioblastoma multiforme (GBM) must undergo extensive chemo-radiation therapy, but quality of life (QoL) during treatment has not been fully evaluated. Patients enrolled in a randomized phase II clinical trial of dasatinib in combination with standard chemo-radiotherapy were asked to complete multiple QoL questionnaires at several assessments. The addition of dasatinib to standard chemo-radiotherapy did not impact patient overall QoL, and results were comparable across the QoL questionnaires. Significant decline in questionnaire compliance was observed secondary to disease progression and health deterioration.

Gastrointestinal / Translational Research

Vitamin D status and survival of metastatic colorectal cancer patients: Results from CALGB/SWOG 80405 (Alliance)

Ng K, Venook AP, Sato K, Yuan C, Hollis BW, Niedzwiecki D, Ye C, Chang IW, O'Neil BH, Innocenti F, Lenz HJ, Blanke CD, Mayer RJ, Fuchs CS Meyerhardt JA. J Clin Oncol 33, 2015 (suppl; abstr 3503)

Synopsis: This evaluation demonstrated that higher plasma vitamin D level is associated with better outcome in metastatic colorectal cancer (mCRC) patients treated with chemotherapy + biologics. Using plasma samples collected from 1,043 patients enrolled on CALGB/SWOG 80405, the investigators showed that comparing to the patients in the lowest quintile, the ones in the highest quintile of 25-hydroxyvitamin D level have improved overall survival (median 32.6 versus 24.5 months) and progression-free survival (median 12.2 versus 10.1 months). This finding has led to a new ongoing randomized trial to explore the benefit of vitamin D supplement and effect of genetic factors in related pathway genes.

Analysis of DNA mismatch repair (MMR) and clinical outcome in stage III colon cancers from patients (pts) treated with adjuvant FOLFOX +/- cetuximab in the PETACC8 and NCCTG N0147 adjuvant trials

Zaanan A, Shi Q, Taieb J, Alberts SR, Smyrk TC, Julie C, Zawadi A, Tabernero J, Mini E, Goldberg RM, Folprecht G, Van Laethem JL, Le Malicot K, Sargent, Laurent-Puig P, Sinicrope FA. J Clin Oncol 33, 2015 (suppl; abstr 3506)

Synopsis: This study aimed to clarify whether DNA mismatch repair (MMR) status is a prognostic biomarker for stage III colon cancer patients or not. MMR protein (MLH1, MSH2, MSH6) expression level and BRAF V600E (gene mutation) status were evaluated on tumors from more than 4,000 patients enrolled on two adjuvant trials testing FOLFOX +/- cetuximab. Multivariate models showed that patients with MMR deficient tumors had similar three-year DFS (75 percent versus 74 percent), time-to-recurrence and overall survival rates as did patients with proficient MMR tumors. This finding has revealed that at least in those two large phase III study patients, MMR status is not prognostic.

Prognostic value of BRAF V600E and KRAS exon 2 mutations in microsatellite stable (MSS), stage III colon cancers (CC) from patients (pts) treated with adjuvant FOLFOX+/- cetuximab: A pooled analysis of 3934 pts from the PETACC8 and N0147 trials

Taieb J, Le Malicot K, Penault-Llorca FM, Bouche O, Shi Q, Thibodeau SN, Tabernero J, Mini E, Goldberg RM, Folprecht G, Van Laethem JL, Sargent DJ, Alberts SR, Laurent-Puig P, Sinicrope FA. J Clin Oncol 33, 2015 (suppl; abstr 3507)

Synopsis: The current study evaluated the prognostic value of BRAF and KRAS mutation status in a well-defined colon cancer (CC) patient population: microsatellite stable (MSS) resected CC stage III colon patients receiving adjuvant FOLFOX +/- cetuximab. About 3,934 MSS tumor tissues collected under N0147 were analyzed for BRAF (V600E) and KRAS (exon 2). Pooled analysis showed that BRAF V600E and KRAS exon 2 mutations were linked to worse outcome. Therefore, it is concluded that BRAF V600E and KRAS exon 2 mutation status are independent prognostic predictors in this patient population setting.

continued on page 9


Alliance Patient Advocate Involvement in Accrual to NCTN Clinical Trials

By Patricia A. Spears
Vice Chair, Alliance Patient Advocate Committee
Peggy Devine
Member, Alliance Patient Advocate Committee

Accrual of participants to all clinical trials is a huge interest and concern of the Alliance patient advocates. At a recent National Cancer Institute Clinical Trials Advisory Committee (NCI-CTAC) meeting, the NCI indicated that between 2000 and 2010 about 24 percent of all adult cancer clinical trials closed with inadequate accrual (<90 percent). This is unacceptable. Even though it has been known and talked about for many years, the lack of adequate accrual persists.

In 2010, the NCI and the American Society of Clinical Oncology (ASCO) held an accrual meeting titled *Clinical Trials Accrual Symposium: Science and Solutions*, in which major stakeholders were gathered to talk about key issues that were contributing to the accrual failure of many NCI clinical trials. The meeting focused on both patient-centered solutions, including patient decision-making, minority and underrepresented populations and community outreach and education, as well as site-centered and national level solutions that would, if implemented, improve accrual. Strategies to meet patient needs, decision aids as well as optimizing communication skills between staff and patients needs to be explored more fully. Communication between the patient and staff was the key to successful accrual.[1]

Recently, the NCI gathered key stakeholders (75 attendees, including five National Clinical Trials Network (NCTN) patient advocates) to talk about accrual to NCTN trials (December 4-5, 2014). The meeting was titled *NCTN Meeting to Address Accrual Challenges in NCTN Clinical Trials in Adults and Adolescents and Young Adults (AYA).* The goals of the meeting were to: 1) develop consensus around key operational accrual challenges in the NCTN and potential strategies to address those challenges, and 2) lay the groundwork for a group devoted to NCTN accrual issues. Most of these solutions focus on operational strategies, with little attention to addressing the needs of individual patients as they are approached about a clinical trial. Both approaches need to be the focus, as it is the patient who signs the consent form, not the staff. A summary of this meeting was recently presented to the patient advocates of all NCTN groups as well as NCI steering committee patient advocates. Furthermore, the work of this group was presented at the 2015 ASCO meeting.[2]

Now what? The NCI has developed a plan, which begins with the creation of a Network Accrual Core Team (ACT), consisting of multiple stakeholders from all NCTN groups, including patient advocate members. ACT is intended to provide the leadership and guidance for all NCTN groups to communicate and collaborate with a focus on accrual. ACT will also oversee multiple topical task forces on trial specific templates, accrual metrics, and NCTN accrual dashboards, amongst others. NCTN patient advocate involvement in this initiative is critical.

We, as patients, see challenges not only with adequate accrual, but also in the lack of diversity of participants who enroll in clinical trials, for real-world representation in all clinical trials.

The patient advocates of all the NCTN groups compiled information from each group and presented shared successes and challenges from the advocate perspective at the recent NCTN meeting. There were systemic issues identified that exacerbate accrual challenges, including inconsistencies of the inclusion of patient advocates in clinical trial development. There are not only inconsistencies among NCTN groups but also within a group among the different committees. Superficial and peripheral involvement of patient advocates translates into a trial opening with little or no assessment of accrual challenges from the patient perspective. Also, there are inconsistencies in the NCTN groups and committees for using the input of the advocates, when the advocates do bring forward key issues.

What is the solution? It's complicated. However, there are things that can be done to enhance our attention to

continued on next page

PATIENT ADVOCATE continued

accrual throughout the continuum of clinical trial development, from the initial idea and throughout the conduct of the trial.

The initiative of the NCI to establish ACT and topical task forces is a great beginning. In addition, continued commitment at the NCTN group level will help address accrual. For example, accrual challenges can be identified while trials are being developed. When identified early they can be addressed more easily than in an ongoing trial which is struggling. The Alliance for Clinical Trials in Oncology uses an accrual checklist that is filled out at concept submission to identify common study designs that can result in accrual challenges. If challenges are identified, the study team is asked for ways in which they will address the potential accrual barrier. This exercise can truly serve a trial well as long as it is fully carried out, with mindfulness to the input of all, including the patient advocates.

Adding consistency and accountability to the process of inclusion of patient advocates in clinical trial development is an important part of addressing accrual. Involving patient advocates early adds value and consistency to the process. The development of an accrual plan, not just an accrual forecast, might improve accrual. A plan that not only identifies challenges but one that enables the study team to address the challenges early, not waiting until the trial is open and there is inadequate accrual.

The Alliance has had accrual initiatives, which have shown some success in terms of improvement of ongoing accrual, or accrual to trials at the rate predicted or higher than predicted. The patient advocates have been a part of these initiatives, through development of materials such as patient brochures, providing exposure for the trial through patient advocacy groups, and involvement in Alliance accrual programs.

Moving forward, communication and collaboration among all stakeholders at all levels will be critical. At the NCTN level, the patient advocates plan to work together to communicate best practices, evaluate the big genomic trials, develop tools for assessment and provide training for patient advocates. Within the Alliance, there are strategies that we can initiate to ensure consistency of patient advocate involvement with the goal of accrual enhancement. Patient advocates of the Alliance are committed to ensure that clinical trials developed in the Alliance are able to complete accrual as predicted, allowing new treatments to be available to every patient more quickly.

Source

1. The National Cancer Institute-American Society of Clinical Oncology Cancer Trial Accrual Symposium: summary and recommendations." J Oncol Pract. 2013 Nov;9(6):267-76. doi: 10.1200/JOP.2013.001119. Epub 2013 Oct 15.
2. "Creating a national collaborative strategy to enhance trial accrual in NCI's National Clinical Trials Network (NCTN) in the era of precision medicine." J Clin Oncol 33, 2015 (suppl; abstr 6589)

Acknowledgment

Thank you to Pat Gavin and Elise Horvath for critical reading and feedback on this article.

SPOTLIGHT ON TRIALS continued from page 1

therapy agents and the response data (pCR rate) to standard chemotherapy for the resistant population, results from this study are expected to provide the foundation for future novel therapeutics development for early stage ER+ breast cancer.

Refer to the study protocol (Alliance A011106), which can be found on the CTSU menu (ctsu.org) for complete information on the trial design, treatment plan and patient eligibility. The Alliance Study Chair is Cynthia Ma, MD, PhD, Washington University School of Medicine, e-mail: cma@dom.wustl.edu.

Source

1. Howlader, N., et al., SEER Cancer Statistics Review, 1975-2008, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2008/, based on November 2010 SEER data submission, posted to the SEER web site, 2011. 2011.
2. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2015. CA Cancer J Clin 2015, 65(1):5-29.
3. Anderson, W.F., et al., Estrogen receptor breast cancer phenotypes in the Surveillance, Epidemiology, and End Results database. Breast Cancer Res Treat, 2002. 76(1): p. 27-36.
4. Demicheli, R., et al., Recurrence and mortality according to estrogen receptor status for breast cancer patients undergoing conservative surgery. Ipsilateral breast tumour recurrence dynamics provides clues for tumour biology within the residual breast. BMC Cancer, 2010. 10: p. 656.
5. Demicheli, R., et al., Recurrence and mortality dynamics for breast cancer patients undergoing mastectomy according to estrogen receptor status: different mortality but similar recurrence. Cancer Sci, 2010. 101(3): p. 826-30.
6. Early Breast Cancer Trialists' Collaborative, G., Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. The Lancet, 2011. 378(9793): p. 771-784.
7. Cuzick, J., et al., Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. The Lancet Oncology, 2010. 11(12): p. 1135-1141.
8. Ellis, M.J., et al., Outcome prediction for estrogen receptor-positive breast cancer based on postneoadjuvant endocrine therapy tumor characteristics. J Natl Cancer Inst, 2008. 100(19): p. 1380-8.

Alliance Cancer Control Program Presents Funding Awards to Nine Investigators

Nine Alliance researchers and junior investigators have been selected to receive annual funding awards to support their work through the Alliance NCI Community Oncology Research Program (NCORP) Research Base, which is supported by the NCI Division of Cancer Prevention (DCP) and administrated through the Alliance Cancer Control Program (CCP). The annual awards include the **Alliance Cancer Control Program Pilot Project Award** and **Alliance Cancer Control Program Junior Faculty Award**.

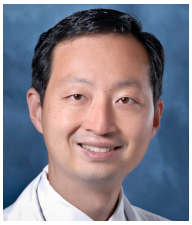
Pilot Project Award

Jatio

Rowland

Gaur

Dragnev



Kim

Aminah Jatoi, MD (Mayo Clinic) and **Kendrith Rowland, MD** (Carle Clinic)
"Curcumin + piperine for uteral stent-induced symptoms in older cancer patients: A pilot study to derive a safe, optimal biological dose"

Arti Gaur, PhD and **Konstantin Dragnev, MD** (Dartmouth Hitchcock Medical Center)
"MicroRNAs as biomarkers of treatment efficacy and toxicity in glioblastoma patients"

Hyung Kim, MD (Cedars Sinai Medical Center)
"Cholesterol lowering intervention for prostate cancer active surveillance"

Junior Faculty Award

Enzinger

In

Noonan

Peters

Andrea Enzinger, MD | Mentor: Deb Schrag, MD (Dana-Farber Cancer Institute)
"Patient centered videos to enhance informed consent for palliative chemotherapy"

Haejin In, MD, MBA, MPH | Mentor: Bruce Rapkin, PhD (Albert Einstein College of Medicine)
"Development of a gastric cancer brief screener to identify persons for screening endoscopy referral"

Devon Noonan, PhD, MPH, FNP-BC | Mentor: Kathryn Pollak, PhD (Duke University School of Nursing)
"Addressing tobacco use disparities in rural older adults through an innovative mobile phone intervention: Testing the feasibility of the texto4gotobacco intervention"

Erica Peters, PhD | Mentor: James Marshall, PhD (Roswell Park Cancer Institute)
"Data harmonization and preliminary analysis for a pooling project of seven completed Alliance trials"

To learn more about the Alliance Cancer Control Program Pilot Project Award and Junior Faculty Award, contact Electra D. Paskett, PhD, CCP Deputy Director, at electra.paskett@osumc.edu.

ALLIANCE MEMBERS ON THE MOVE

Grubbs

Stephen Grubbs, MD, has been named the Senior Director of the American Society of Clinical Oncology's (ASCO) new Clinical Affairs Department. Dr. Grubbs is the former Principal Investigator of the Delaware Christiana Care National Cancer Institute (NCI) Community Oncology Research Program (NCORP) and Managing Partner at Medical Oncology Hematology Consultants, PA. He is also active in the Alliance for Clinical Trials in Oncology, serving on the Board of Directors and Executive Committee. Under Dr. Grubbs' leadership, the new department will provide services, education and resources to support oncology practices in all settings. It also will promote the delivery of high quality, high value cancer care for people with cancer by providing tools and services to facilitate innovation in cancer care delivery and respond to growing economic and administrative challenges in oncology practice. In addition, the department will provide national support in business analytics, performance improvement, and practice management to oncology professionals.

Perez

Edith A. Perez, MD, has been elected to the American Association for Cancer Research (AACR) Board of Directors for the 2015-2018 term. Dr. Perez is Group Vice Chair of the Alliance for Clinical Trials in Oncology, Deputy Director at Large for Mayo Clinic Cancer Center, and the Serene M. and Frances C. Durling Professor of Medicine at Mayo Medical School. She is also Chair of the Mayo Clinic Breast Cancer Translational Genomics Program and Chair of the Breast Cancer Specialty Council. As a cancer specialist, she is an internationally known translational researcher who has developed, and is involved in, a wide range of clinical trials exploring the use of new therapeutic agents for the treatment and prevention of breast cancer. She leads and has helped develop basic research studies to evaluate the role of genetic markers in the development and aggressiveness of breast cancer.

Schapira

Lidia Schapira, MD, FASCO, has been appointed Editor-in-Chief of Cancer.Net, ASCO's patient information website. Dr. Schapira is an Associate Professor of Medicine at Harvard Medical School and a medical oncologist at the Massachusetts General Hospital Cancer Center. She also serves as a senior investigator in research focused on young women with breast cancer. In her new role, Dr. Schapira will continue her innovative work in patient communication. She has collaborated with experts in neuroscience and psychology, investigated new ways to improve the therapeutic connection between patients and clinicians, and worked with cancer researchers, social scientists, and patient advocates to explore and address some of the root causes of disparities in cancer care. As a result of her work, Dr. Schapira developed workshops for community health workers designed to raise awareness of and interest in cancer clinical trials among underserved minorities.

SPOTLIGHT ON TRIALS continued from page 2

10. Smallridge RC, Ain KB, Asa SL, et al. 2012 American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid. 22:1104-1139.
11. Smallridge RC 2012 Approach to the patient with anaplastic thyroid carcinoma. J Clin Endocrinol Metab. 97:2566-2572.
12. Hunt JL, Tometsko M, LiVolsi VA, Swalsky P, Finkelstein SD, Barnes EL 2003 Molecular evidence of anaplastic transformation in coexisting well-differentiated and anaplastic carcinomas of the thyroid. Am J Surg Pathol. 27:1559-1564.
13. Mazzanti C, Zeiger MA, Costourous N, et al. 2004 Using gene expression profiling to differentiate benign versus malignant thyroid tumors. Cancer Res. 64:2898-2903.
14. Onda M, Emi M, Yoshida A, et al. 2004 Comprehensive gene expression profiling of anaplastic thyroid cancers with cDNA microarray of 25 344 genes. Endocr Relat Cancer. 11:843-854.
15. Williams SF, Smallridge RC 2004 Targeting the ERK pathway: novel therapeutics for thyroid cancer. Curr Drug Targets Immune Endocr Metabol Disord. 4:199-220.
16. Michalik L, Auwerx J, Berger JP, Chatterjee VK, Glass CK, Gonzalez FJ, Grimaldi PA, Kadowaki T, Lazar MA, O'Rahilly S, Palmer CN, Plutzky J, Reddy JK, Spiegelman BM, Staels B, Wahli W (2006). "International Union of Pharmacology. LXI. Peroxisome proliferator-activated receptors". Pharmacol. Rev. 58 (4): 726–41. doi:10.1124/pr.58.4.5. PMID 17132851.
17. Martelli ML, Iuliano R, Le Pera I, et al. 2002 Inhibitory effects of peroxisome poliferator-activated receptor gamma on thyroid carcinoma cell growth. J Clin Endocrinol Metab. 87:4728- 4735.
18. Belfiore A, Genua M, Malaguarnera R (2009). "PPAR-gamma Agonists and Their Effects on IGF-I Receptor Signaling: Implications for Cancer". PPAR Res 2009: 830501. doi:10.1155/2009/830501. PMC 2709717. PMID 19609453.
19. Berger J, Moller DE (2002). "The mechanisms of action of PPARs". Annu. Rev. Med. 53: 409–35. doi:10.1146/annurev.med.53.082901.104018. PMID 11818483.
20. Feige JN, Gelman L, Michalik L, Desvergne B, Wahli W (2006). "From molecular action to physiological outputs: peroxisome proliferator-activated receptors are nuclear receptors at the crossroads of key cellular functions". Prog. Lipid Res. 45 (2): 120–59. doi:10.1016/j.plipres.2005.12.002. PMID 16476485.
21. Lu M, Kwan T, Yu C, et al. 2005 Peroxisome proliferator-activated receptor gamma agonists promote TRAIL-induced apoptosis by reducing survivin levels via cyclin D3 repression and cell cycle arrest. J Biol Chem. 280:6742-6751.
22. Liu D, Xing M 2008 Potent inhibition of thyroid cancer cells by the MEK inhibitor PD0325901 and its potentiation by suppression of the PI3K and NF-kappaB pathways. Thyroid. 18:853-864.
23. Ling X, Bernacki RJ, Brattain MG, Li F 2004 Induction of survivin expression by taxol (paclitaxel) is an early event, which is independent of taxol-mediated G2/M arrest. J Biol Chem. 279:15196-15203.
24. Tirro E, Consoli ML, Massimino M, et al. 2006 Altered expression of c-IAP1, survivin, and Smac contributes to chemotherapy resistance in thyroid cancer cells. Cancer Res. 66:4263-4272.
25. Ito Y, Yoshida H, Uruno T, et al. 2003 Survivin expression is significantly linked to the dedifferentiation of thyroid carcinoma. Oncol Rep. 10:1337-1340.

ALLIANCE @ANNUAL MEETINGS continued from page 4

Influence of molecular alterations on site-specific (SS) time to recurrence (TTR) following adjuvant therapy in resected colon cancer (CC) (Alliance Trial N0147)

Wilcox RE, Shi Q, Sinicrope FA, Sargent DJ, Foster NR, Meyers JP, Goldberg RM, Nair S, Shields AF, Chan E, Gill S, Kahlenberg MS, Alberts SR. J Clin Oncol 33, 2015 (suppl; abstr 3590)

Synopsis: This study searched for molecular biomarkers of site-specific time to recurrence (ssTTR) in resected stage III colon cancer patients. Various genetic markers MMR, KRAS exon 2, BRAF V600E were evaluated in 3,098 patients enrolled on N0147 and the association between biomarker and ssTTR were tested. This finding revealed that status of MMR and BRAF, influences site of recurrence and TTR; but interestingly, not KRAS alone.

A genome-wide association study (GWAS) of overall survival (OS) in 609 metastatic colorectal cancer (mCRC) patients treated with chemotherapy and biologics in CALGB 80405

Innocenti F, Owzar K, Jiang C, Sibley A, Niedzwiecki D, Lenz HJ, Bertagnolli MM, Friedman PN, Furukawa Y, Kubo M, Ratain MJ, Blanke CD, Venook AP, McLeod HL. J Clin Oncol 33, 2015 (suppl; abstr 3599)

Synopsis: In this first large genome-wide association study conducted in metastatic colorectal cancer (mCRC) patients receiving standard of care treatment, germline genetic predictors for overall survival is evaluated using 609 germline DNA samples collected under CALGB/SWOG 80405. GWAS analysis revealed three single nucleotide polymorphisms (SNP), including one intronic variant in AXIN1 gene. A common SNP (G to A) in the AXINI gene results in worse overall survival. Interestingly, AXINI is known as a negative regulator for the WNT pathway in CRC through interaction with APC. However, this finding needs further replication and validation effort.

Upcoming Meeting Dates

2015
Fall Group Meeting
November 4-8

2016
Fall Group Meeting
November 2-5

2017
Fall Group Meeting
November 1-4

All meetings are open to all Alliance members and will be held at
Loews Chicago O'Hare Hotel, 5300 N. River Road, Rosemont, IL 60018

For meeting and travel inquiries
contact Alison Lewandowski | **e-mail** alewandowski@partners.org
phone 617-525-3022 | **website** AllianceforClinicalTrialsinOncology.org