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-- PRESS BRIEFING MONDAY, JUNE 1, 11:00 AM EDT --

STUDIES SHED LIGHT ON CRITICAL CHALLENGES IN CANCER RESEARCH AND CARE

Orlando, Fla. — Studies examining ongoing controversies in the field of clinical oncology were released today at a press briefing of the 45th Annual Meeting of the American Society of Clinical Oncology (ASCO).

"There are many ongoing debates in cancer research and care, and the best care for our patients is not always clear-cut," said Julie Gralow, MD, an associate professor in the oncology division of the University of Washington School of Medicine and moderator of the press briefing. "The studies presented today shed light on ongoing controversies in the field, and on the challenges physicians face when launching clinical trials, evaluating trial results, advising patients on screening, and determining the most appropriate treatment."

Studies highlighted in the press briefing include:

- *Lung cancer screening:* The effectiveness of lung cancer screening in reducing death rates has been widely debated in recent years. A new study finds that lung cancer screening using low-dose computed tomography results in a high rate of false positives (33 percent after two screenings) and significant follow-up testing, data that should help people at high risk for the disease, make informed decisions about screening.

- *Impact of common antidepressants on tamoxifen effectiveness:* Hot flashes are a common side-effect of tamoxifen treatment to prevent breast cancer recurrence, and are often managed with the antidepressant drugs Paxil and Prozac. Two new studies report differing results about whether these antidepressants have an adverse impact on the effectiveness of tamoxifen. Additional research is needed to resolve these differences, though women may want to consider alternative antidepressants in the meantime.

- *Treatment of breast cancer micrometastases:* Not all women with breast cancer undergo surgery to remove all of the axillary (underarm) lymph nodes upon detection of tiny micrometastases in the lymph node nearest the tumor (the "sentinel" node), given a lack of conclusive data to date demonstrating the effectiveness of such treatment. However, a new study finds significantly higher rates of cancer recurrence among women with micrometastases who do not undergo axillary lymph node dissection, supporting routine use of the procedure to prevent the return of cancer.

- More -

- *Patient accrual in clinical trials:* Low rates of patient enrollment in cancer clinical trials have been an ongoing challenge in cancer research, with just five percent of cancer patients participating. A new analysis of federally-funded cancer trials finds that a full 40 percent of trials examined did not meet their enrollment goals, threatening their ability to report statistically significant results. The study found that the longer a trial takes to develop, the less likely it is to meet its accrual goal, emphasizing the importance of finding ways to shorten clinical trial development time.

For consumer-oriented information on these studies and more than 120 cancer types, please refer your readers to ASCO's patient website, www.Cancer.Net.

This study is embargoed for release until Saturday, May 30 at 3:45 PM EDT

ORAL PRESENTATION
SATURDAY, MAY 30, 3:45 PM EDT
LEVEL 2, W203C
CANCER PREVENTION

Lead Author: Jennifer M. Croswell, MD
National Institutes of Health
Bethesda, Md.

Lung Cancer Screening by Low-Dose Computed Tomography Results in High Rate of False Positives

Researchers from the National Institutes of Health (NIH) have shown that patients who undergo lung cancer screening with low-dose computed tomography (LDCT) are at high risk for receiving false-positive results.

Several studies evaluating whether lung cancer screening reduces cancer deaths have reported a high incidence of noncalcified nodules (round lesions of unknown cause) among those screened. However, this study marks the first time that the cumulative risk of a false-positive result has been quantified.

The study included 1,610 patients who underwent LDCT screenings and 1,580 who underwent chest x-ray. Participants were between 55 and 74 years old and current or former smokers. They underwent a baseline screening exam, a follow-up exam at one year, and were followed for an additional year. For a patient choosing to undergo LDCT, the risk of obtaining a false-positive result is 21 percent after one scan and 33 percent after a second. Patients choosing to undergo chest x-ray screening have a false-positive risk of 9 percent after one test and 15 percent after two. False-positive results were defined as noncalcified nodules greater than or equal to 4 mm or other findings that indicated a suspicion of cancer that were later found to be noncancerous.

Of the patients who had false positives, slightly more than half underwent follow-up imaging exams. In the LDCT group, 6.6 percent of patients with false positives underwent invasive diagnostic procedures and 1.6 percent had major surgery. In the x-ray group, 4.2 percent of patients with false positives underwent invasive follow-up procedures and 1.9 percent of the total patients in this group had major surgery. Complication rates for patients who had invasive procedures were low, but a few patients had to be hospitalized for a collapsed lung or blood in the lung (less than 1 percent), and another 1 percent had to be given antibiotics for infections.

“All medical interventions – including screenings – have not only the potential to benefit patients but also the potential for harm,” said Jennifer M. Croswell, MD, Acting Director of the NIH Office of Medical Applications of Research and the study’s lead author. “We want to give people who are considering lung cancer screening the information they need to make informed decisions about the tests they choose. False-positive results may create increased psychological stress in patients and an increased burden on the healthcare system.”

Findings from the study indicated that patients who were current smokers or older than 64 years of age might have an increased risk of false positives, but because the sample sizes were small, the researchers say more studies are needed to confirm those findings.

CRA1502

Cumulative risk for a false-positive test using low-dose computed tomography in lung cancer screening

J. M. Croswell, S. G. Baker, P. M. Marcus, J. D. Clapp, B. S. Kramer

Background: Screening with low-dose computed tomography (LDCT) has been promoted as the best hope for curing lung cancer. However, cumulative false-positive (FP) rates have never been formally reported. We quantified the cumulative risk of receiving ≥1 FP test for individuals in a lung cancer screening program with 2 annual screens. **Methods:** Prior to the ongoing National Lung Screening Trial (NLST), a definitive randomized controlled trial of LDCT versus single-view chest xray (CXR), a randomized controlled feasibility trial was conducted at six NLST centers. Participants (55-74 years at entry, current or former smokers, and ≥ 30 pack/year smoking history) were offered a baseline LDCT (N = 1,610) or CXR (N = 1,580), and one repeat annual screen, and were followed for 1 year after their final screen. Participants who received at least one screening exam were eligible for this analysis. Exclusion criteria included chest CT in the past 24 months or history of lung cancer. A positive screen was any noncalcified nodule ≥ 4 mm or other radiographic finding deemed suspicious for cancer. A FP was a positive screen with: 1) a completed negative work-up, or 2) ≥ 12 months follow-up with no cancer diagnosis. **Results:** Using a Kaplan-Meier analysis, an individual’s cumulative probability of ≥ 1 FP LDCT was 21% (95% CI, 19%-23%) after one screen and 33% (95% CI, 30%-35%) after two. The cumulative probability of ≥ 1 FP CXR was 9% (95% CI, 8%-11%) and 15% (95% CI, 13%-16%) after one and two screens, respectively. On multivariable analysis, higher odds of FP for LDCT were associated with increased participant age (>64 years) (OR 1.34, 95% CI, 1.04-1.73); current versus former smoker status trended toward higher FP odds (OR 1.22, 95% CI, 0.95-1.56). 6.6% of participants with a FP LDCT underwent an

invasive diagnostic follow-up procedure; 1.6% had major surgery. 4.2% of participants with a FP CXR underwent an invasive diagnostic follow-up procedure; 1.9% had major surgery. **Conclusions:** Risks of LDCT FP are substantial after only two annual examinations; the potential resulting economic, psychosocial, and physical burdens of this modality warrant investigation.

Both studies are embargoed for release until Saturday, May 30 at 4:00 PM EDT

ORAL PRESENTATION
SATURDAY, MAY 30, 3:45 PM EDT
LEVEL 2, WEST HALL D1
BREAST CANCER – LOCAL-REGIONAL AND ADJUVANT THERAPY

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Studies Report Mixed Findings on Whether Common Drugs for Hot Flashes Impact Effectiveness of Tamoxifen for Preventing Breast Cancer Recurrence

Two retrospective studies report mixed results on whether a class of drugs known as 2D6 inhibitors reduce the effectiveness of tamoxifen for preventing breast cancer recurrence.

In the body, tamoxifen is broken down to several active compounds; endoxifen is one of the most biologically active of these metabolites. Previous research has shown women who have a gene mutation that prevents them from making the 2D6 enzyme, which converts tamoxifen to endoxifen, do not get the same benefit from tamoxifen as women with a normal version of the gene. Other studies have suggested that drugs that inhibit the 2D6 enzyme reduce blood levels of endoxifen in women taking tamoxifen.

2D6 inhibitors include a variety of drugs, but the two most common are fluoxetine (Prozac) and paroxetine (Paxil). These drugs, known as selective serotonin reuptake inhibitors (SSRIs), have often been prescribed to reduce hot flashes caused by tamoxifen. (They are also commonly used to treat depression). Similar drugs can be used to treat both hot flashes and depression that do not inhibit 2D6.

U.S. study finds women taking 2D6 inhibitors with tamoxifen have higher rates of breast cancer recurrence

(Note: Includes updated data not in the abstract.)

This study, conducted by the U.S. pharmacy benefit management company Medco, examined women in Medco's database who were treated for breast cancer and then initiated and were adherent to tamoxifen therapy to prevent recurrence. The study identified 945 women who took tamoxifen alone and an additional 353 who were treated with both tamoxifen and a 2D6 inhibitor (the most common of these were paroxetine and fluoxetine).

The researchers found that women taking tamoxifen alone had a recurrence rate of 7.5 percent over a two-year period, compared with a 13.9 percent recurrence rate for women taking tamoxifen and a 2D6 inhibitor. The average time of overlap when both drugs were taken was 255 days.

"These findings suggest that some drugs commonly prescribed to help reduce hot flashes associated with tamoxifen therapy may be decreasing the effectiveness of their anti-cancer treatment," said Robert Epstein, MD, Chief Medical Officer at Medco and one of the study's authors. "If women are taking tamoxifen and need an SSRI to reduce their hot flashes, there are other SSRI drug options that don't inhibit 2D6 or result in the higher recurrence rates."

Dutch study finds 2D6 inhibitors have little effect on breast cancer recurrence rate

A study from Holland analyzed data from three national databases, and identified 1,962 women who were treated with tamoxifen following surgery for early-stage breast cancer. The researchers found that about 11 percent had taken a 2D6 inhibitor at some point while they were also taking tamoxifen.

After a median follow-up time of 4.1 years (for patients who are event-free at time of analysis), the researchers found that among women who took tamoxifen alone or took a 2D6 inhibitor for less than 60 days (1,812 women),

14.6 percent experienced a recurrence. Among patients who took tamoxifen at the same time as a 2D6 inhibitor for 60 days or more (150 women), 13.3 percent experienced a breast cancer recurrence.

"Based on our findings and previous studies, we don't have strong evidence that it's unsafe to use 2D6 inhibitors during tamoxifen therapy," said Vincent O. Dezentjé, MD, a trainee in oncology at Leiden University Medical Center and the study's first author. "But because the number of patients on both tamoxifen and 2D6 inhibitors was small in our study (and because of a possible confounding or modifying effect of CYP2D6 genotype), our findings will need to be confirmed in larger trials. Until a link between 2D6 inhibitors can be definitively confirmed, doctors and patients should be cautious about using these drugs together."

CRA508

Risk of breast cancer recurrence in women initiating tamoxifen with CYP2D6 inhibitors

R. E. Aubert, E. J. Stanek, J. Yao, J. R. Teagarden, M. Subar, R. S. Epstein, T. C. Skaar, Z. Desta, D. A. Flockhart

Background: Tamoxifen (TAM) is metabolized to its active form, endoxifen, by hepatic cytochrome P450 (CYP) 2D6. Diminished CYP2D6 function, both by genetic variation or concurrent use of pharmacologic inhibitors, can significantly reduce endoxifen plasma concentrations and may lead to reduced TAM effectiveness. **Methods:** We interrogated an integrated research database comprised of de-identified medical and pharmacy claims (Rx) data for 10.7 million U.S. health plan members to identify women with breast cancer (BrCa) new to TAM therapy in a 30-month period from 2003 to 2005, and investigated the risk of recurrent BrCa as a function of concurrent use of potent and moderate inhibitors of CYP2D6. Inclusion criteria were: greater than or equal to 24 months of follow-up data and adherence to TAM (medication possession ratio $\geq$ 70%) over 2 years (N = 1298). Disease recurrence was defined by BrCa ICD-9 codes or CPT codes for mastectomy, lumpectomy, lymph node dissection, or radiation therapy occurring at least 6 months after the index TAM Rx. Two study groups were identified: TAM alone (N = 945) or TAM + a CYP2D6 inhibitor concomitantly (N = 353). BrCa recurrence rates were compared using Kaplan-Meier analysis with log-rank test, and univariate hazard ratios (HR) with 95% confidence intervals (CI) were estimated by Cox proportional hazards model. **Results:** The study groups were similar at baseline. Median age was 52 years (TAM) and 53 years (TAM + CYP2D6 inhibitor). Interventions performed in the TAM alone group included mastectomy in 54%, lumpectomy in 36%, and radiation therapy in 47%, and were 52%, 38%, 46%, respectively, in the TAM + CYP2D6 inhibitor group. Among women on a CYP2D6 inhibitor, the median duration of overlap with TAM was 255 days. Patients receiving TAM + a CYP2D6 inhibitor had a 2-year BrCa recurrence rate of 13.9% versus 7.5% in patients receiving TAM alone (HR 1.92, 95% CI 1.33-2.76, $p < 0.001$). **Conclusions:** Our findings support the presence of a clinically significant drug interaction between TAM and known CYP2D6 inhibitors. This resulted in a significant 1.9 fold higher BrCa recurrence within 2 years of initiating TAM therapy.

Disclosures: Ronald Aubert,,Employment or Leadership Position,Medco Health Solutions, Inc.Ronald Aubert,,Stock Ownership,Medco Health Solutions, Inc.Eric Stanek,,Stock Ownership,Medco Health Solutions, Inc.Eric Stanek,,Employment or Leadership Position,Medco Health Solutions, Inc.Jianying Yao,,Employment or Leadership Position,Medco Health Solutions, Inc.Jianying Yao,,Stock Ownership,Medco Health Solutions, Inc.J Teagarden,,Employment or Leadership Position,Medco Health Solutions, Inc.J Teagarden,,Stock Ownership,Medco Health Solutions, Inc.Milayna Subar,,Employment or Leadership Position,Medco Health Solutions, Inc.Milayna Subar,,Stock Ownership,Medco Health Solutions, Inc.Robert Epstein,,Stock Ownership,Medco Health Solutions, Inc.Robert Epstein,,Employment or Leadership Position,Medco Health Solutions, Inc.Todd Skaar,,Honoraria,Roche Molecular Systems, Inc.David Flockhart,,Consultant or Advisory Role,Roche Molecular DiagnosticsDavid Flockhart,,Consultant or Advisory Role,Medco Health Solutions, Inc.David Flockhart,,Consultant or Advisory Role,LabCorp

CRA509

Concomitant CYP2D6 inhibitor use and tamoxifen adherence in early stage breast cancer: A pharmacoepidemiological study

V. Dezentje, N. J. Van Blijderveen, H. Gelderblom, H. Putter, M. P. Van Herk - Sukel, M. K. Casparie, A. C. Egberts, J. W. Nortier, H. J. Guchelaar

Background: The use of cytochrome P450 2D6 inhibiting drugs (CYP2D6 inhibitors) during tamoxifen treatment leads to a decrease in plasma concentration of endoxifen, the major active tamoxifen metabolite. Concomitant use of CYP2D6 inhibitors, such as the commonly prescribed selective serotonin reuptake inhibitors, as well as low tamoxifen adherence may negatively impact tamoxifen efficacy in breast cancer. The objectives were to relate concomitant CYP2D6 inhibitor use and tamoxifen adherence to breast cancer event free time (EFT). **Methods:** Data were used from PHARMO, a pharmacy database, PALGA, a nationwide pathology database and the Dutch Medical Register in the Netherlands. Breast cancer patients who were treated with tamoxifen as adjuvant therapy between 1994 and 2006 were included. A Cox proportional hazards model with a time-dependent definition for the CYP2D6 inhibitor exposure was used. **Results:** 1,990 breast cancer patients using tamoxifen were included, among whom 215 (10.8%) used a CYP2D6 inhibitor during tamoxifen treatment. No association between concomitant CYP2D6 inhibitor use and breast cancer recurrence was observed. Poor tamoxifen adherence was associated with lower EFT. **Conclusions:** This observational study did not show an association between concomitant CYP2D6 inhibitor use and breast cancer recurrence among patients treated with adjuvant tamoxifen. However, this study shows for the first time that poor tamoxifen adherence is associated with lower EFT.

This study is embargoed for release until Saturday, May 30 at 3:00 PM EDT

ORAL PRESENTATION
SATURDAY, MAY 30, 3:00 PM EDT
LEVEL 2, WEST HALL D1
BREAST CANCER – LOCAL-REGIONAL AND ADJUVANT THERAPY

Lead Author:
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Sentinel Node Micrometastases Strongly Indicate Need for Additional Treatment in Patients with Breast Cancer

A group of Dutch researchers has found that women with early-stage breast cancer who have micrometastases in the sentinel lymph node have a significantly higher rate of recurrence if they do not receive follow-up treatment on additional axillary lymph nodes (those under the arm). They also report that about one in ten doctors are not treating these very small metastases.

For patients with early-stage breast cancer, physicians examine the sentinel lymph node to determine the extent that cancer has spread and whether additional treatment is needed in the remaining axillary lymph nodes. Treatment generally involves a second operation to remove the axillary lymph nodes, but radiation therapy is also used. For macrometastases – metastases greater than 2.0 mm – evidence of the need for further treatment has been clear. Evidence has been less certain, however, for patients with micrometastases – metastases between 0.2 mm and 2.0 mm, and for patients with isolated tumor cells (individual cells or tumor cell clusters smaller than 0.2 mm).

"We found that about 10 percent of doctors are not treating micrometastases. This is most likely due to concern about overtreatment and a lack of clear data on these very small metastases, but our study provides explicit evidence that foregoing treatment for micrometastases results in high cancer recurrence rates. We hope these findings will be a tipping point for doctors not currently treating women for this stage of cancer," said Vivianne Tjan-Heijnen, MD, PhD, a professor of medical oncology at the Maastricht University Medical Center in the Netherlands and the study's lead author. "Additionally, our study suggests that radiation therapy is a good alternative to surgery, which could spare many women additional recovery, although more data to confirm these findings are warranted."

This retrospective study included about 2,700 women who underwent surgery for early-stage breast cancer between 1997 and 2005 and had a sentinel node biopsy that showed no evidence of macrometastases. Women were then divided into three groups: Those with no tumor cells in the sentinel node, those with isolated tumor cells, and those with micrometastases. All women either underwent no additional treatment, surgery to remove remaining axillary nodes, or radiation therapy to the axillary nodes.

For patients with micrometastases, the five-year recurrence rate in the axillary nodes was 4.5 times higher for patients who had no additional treatment than for patients who had either surgery or radiation. Additional axillary treatment did not significantly improve recurrence rates among women with either no tumor cells or only isolated tumor cells in the sentinel node.

Until further studies addressing the clinical relevance of isolated tumor cells or micrometastases in the SLN are complete, the Panel recommends routine ALND for patients with micrometastases (>0.2 ≤2 mm) found on SNB, regardless of the method of detection.

CRA596
Impact of omission of completion axillary lymph node dissection (cALND) or axillary radiotherapy (ax RT) in breast cancer patients with micrometastases (pN1mi) or isolated tumor cells (pN0[i+]) in the sentinel lymph node (SN): Results from the MIRROR study
V. C. Tjan-Heijnen, M. J. Pepels, M. de Boer, G. F. Borm, J. A. van Dijck, C. H. van Deurzen, E. M. Adang, M. B. Menke-Pluymers, P. J. van Diest, P. Bult
Background: The Dutch MIRROR study is the largest cohort study on pN1mi and pN0(i+) in the SN era with long-term follow-up, central pathology review (6th AJCC-classification), and separate analyses on the use of adjuvant systemic therapy (AST). In patients not receiving AST, pN1mi and pN0(i+) as final N-stage were shown to be independent prognosticators for disease-free survival (SABCS 2008, #23, oral). As a substantial number of patients in the MIRROR

study did not undergo cALND or ax RT, we questioned whether this policy was safe in patients with pN1mi(sn) or pN0(i+)(sn). **Methods:** Patients operated for breast cancer in all Dutch hospitals in the years 1998-2005, having favorable primary tumor characteristics, and having undergone an SN biopsy without macrometastases as final N-stage were included. For this present research question, patients were categorized by their SN-stage. Median follow-up was 4.7 years. The Kaplan-Meier method was used to estimate 5-year axillary recurrence (AR) rates, and Cox regression was used to estimate the hazard ratios (HR). In the analyses, the effect of AST was taken into account. **Results:** In total, 835 patients with pN0(i-)(sn), 799 patients with pN0(i+)(sn), and 958 patients with pN1mi(sn) were included. AR rates, and HRs on AR are displayed below. **Conclusions:** Omission of cALND or ax RT in patients with pN1mi(sn) resulted in a significantly higher 5-year AR rate, even after correction for AST, and other patient and tumor characteristics. This indicates that patients with pN1mi(sn) should undergo cALND or ax RT to prevent AR. Support: The Netherlands organization for health research and development (ZonMw), and the Dutch Breast Cancer Trialists' Group (BOOG).

	n	5-year AR(%)	HR AR (95% CI)*
pN0(i-)(sn) cALND	113	1.9	1.00
pN0(i-)(sn) SN	722	2.2	1.07 (0.23 - 4.94)
pN0(i+)(sn) cALND or ax RT	459	1.1	1.00
pN0(i+)(sn) SN	340	1.7	2.14 (0.57 - 7.96)
pN1mi(sn) cALND or ax RT	828	1.2	1.00
pN1mi(sn) SN	130	6.2	4.45 (1.46 - 13.54)
* Corrected for AST, age, (log) tumor size, grade, hormone receptor status.			

This study is embargoed for release until Sunday, May 31 at 8:00 AM EDT

POSTER DISCUSSION
SUNDAY, MAY 31, 11:30 AM EDT
LEVEL 2, W203C
HEALTH SERVICES RESEARCH

Lead Author: Steven K. Cheng, PhD
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Longer Development Time for Cancer Clinical Trials Linked to Poorer Performance in Achieving Accrual Goals

New research shows that the longer it takes to develop a cancer clinical trial, the less likely it is that the trial will meet its goal for accruing patients and the less able it will be to report a statistically significant result. The study also found that 40 percent of more than 550 trials examined did not achieve the originally intended accruals as specified by the study design. Of Phase III trials that took more than 27 months, only 7 percent achieved their accrual goal.

"Delays in opening a clinical trial are more than administrative nuisances, they hinder the understanding and treatment of cancer," said Steven K. Cheng, PhD, a postdoctoral fellow at the Center for Management Research Management in Healthcare in the Knight Cancer Institute at the Oregon Health and Science University, and the study's lead author. "Delays in clinical trials are a big disappointment for providers who want to help their patients access promising new treatments. Major barriers previously identified by our center's research include those found in budgeting, contracting, and redundant scientific reviews."

In this study, investigators reviewed all therapeutic, non-pediatric clinical trials developed between 2000 and 2007 and sponsored by the National Cancer Institute's (NCI) Cancer Therapy Evaluation Program (CTEP), which account for about half of all oncology-related clinical trials in the United States. The study included 553 Phase I, I/II, II, and III trials that together enrolled more than 50,000 patients. Development time was defined as the time from initial CTEP submission of the concept to the time the trial began enrolling patients. The median time to develop a clinical trial in oncology was found to be 15 months.

Overall, 40 percent of all CTEP-approved, non-pediatric, treatment trials did not achieve their minimum accrual goals. Studies that were developed relatively quickly (within 9 to 12 months) were significantly more likely to reach their minimum goal, with 77 percent achieving their goal. Of those studies that took the longest time to develop (more than 27 months), just 22 percent achieved minimum accrual. Overall, nearly 8,700 patients who agreed to participate in clinical trials were enrolled in trials that did not achieve their minimum projected accrual goal at study closure.

A major limitation of this study is that it only investigated the single endpoint of achievement of accrual goal; trials can be halted before the endpoint for a variety of other causes, and lack of accrual does not necessarily mean that the trial did not report results. Additionally, the study only included cooperative NCI-CTEP trials, and not trials sponsored by pharmaceutical companies or those that were investigator-initiated. In addition, there was a lack of detail available regarding the decision for closure. Research is currently underway by the center to identify ways to dramatically shorten cancer clinical trial development times, coupled with evaluations of whether those changes improved accrual.

CRA6509

A sense of urgency: Evaluating the link between clinical trial development time and the accrual performance of CTEP-sponsored studies

S. Cheng, M. Dietrich, S. Finnigan, A. Sandler, J. Crites, L. Ferranti, A. Wu, D. Dilts

Background: Post-activation barriers to oncology clinical trial accruals are well documented; however, potential barriers prior to trial opening are not. We investigate one such barrier: trial development time. **Methods:** National Cancer Institute Cancer Therapy Evaluation Program (NCI-CTEP)sponsored trials for all therapeutic, non-pediatric Phase I, I/II, II, and III studies activated in an eight year period (2000-2007) were investigated (n=553). Successful trials were those achieving 100% of minimum accrual goal. Time to open a study was the calendar time from initial CTEP submission to trial activation. Multivariable logistic regression analysis was used to calculate unadjusted and adjusted odds ratios, controlling for study phase and size of expected accruals. **Results:** 40.0 percent (n=221) of CTEP-approved oncology trials failed to achieve minimum accrual goals, with 49.2 percent (n=30) of Phase III trials failing to achieve at least 25 percent of accrual goals. A total of 8,723 patients (17.0% of accruals) accrued to those studies that were unable to achieve the projected minimum accrual goal. Trials requiring 9-12 months development were significantly more likely to achieve accrual goals (odds ratio, 1.94; 95% CI, 1.06 to

3.52, P=0.031) than trials requiring the median time (15-18 months); trials that exceeded 27 months of development time were significantly less likely of achieving accrual goals (odds ratio, 0.14; 95% CI, 0.04 to 0.54, P=0.004). **Conclusions:** A large percentage of oncology clinical trials do not achieve minimum projected accruals. Trial development time appears to be one important predictor of the likelihood of successfully achieving the minimum accrual goals.

Unadjusted and Adjusted Odds Ratio for Achieving Minimum Accrual Goals

Development Time Interval (months)	**Unadjusted Analysis Odds Ratio (95% CI); P Value**	**Adjusted Analysis Controlling for Projected Minimum Accrual Odds Ratio (95% CI); P Value**	**Adjusted Analysis Controlling for Phase of Trial Odds Ratio (95% CI); P Value**
[0,9)	1.20 (0.55 - 2.59); P=0.650	1.17 (0.54 - 2.54); P=0.686	1.13 (0.52 - 2.46); P=0.758
[9,12)	1.94 (1.06 - 3.52); P=0.010	1.96 (1.07 - 3.57); P=0.029	1.86 (1.02 - 3.40); P=0.044
[12,15) (referent)	1.0	1.0	1.0
[18,21)	0.52 (0.27 - 1.00); P=0.051	0.54 (0.27 - 1.05); P=0.068	0.55 (0.28 - 1.07); P=0.078
[21,24)	0.78 (0.39 - 1.57); P=0.482	0.78 (0.38 - 1.57); P=0.478	0.75 (0.37 - 1.53); P=0.435
[24,27)	0.52 (0.20 - 1.35); P=0.179	0.54 (0.21 - 1.40); P=0.205	0.53 (0.20 - 1.37); P=0.191
[27,30)	0.14 (0.04 - 0.54); P=0.004	0.15 (0.04 - 0.58); P=0.006	0.16 (0.04 - 0.59); P=0.006
[30,)	0.17 (0.07 - 0.41); P<0.001	0.18 (0.07 - 0.44); P<0.001	0.19 (0.08 - 0.46); P<0.001

Referent indicates median development time of all clinical trials in the sample

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Moderator Dr. Gralow made the following disclosures: Honoraria from Genentech, Novartis and Roche; Research funding from Amgen, Bayer, Bristol Myers, Genentech, Novartis, Roche and sanofi aventis.

ATTRIBUTION TO THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING IS REQUESTED IN ALL NEWS COVERAGE.

# # #

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