ONCE DEEMED A “FUNCTIONAL WASTELAND,” Y CHROMOSOME IS FOUND TO PLAY A ROLE IN CANCER IMMUNITY

The finding may alter biology textbooks.

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Once deemed a “functional wasteland,” Y chromosome is found to play a role in cancer immunity

The finding may alter biology textbooks

Dan Theodorescu, MD, PhD
Director, Samuel Oschin Comprehensive Cancer Institute,
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Theodorescu spoke with Jacquelyn Cobb, a reporter with The Cancer Letter.
Scientists used to dismiss the notion that the Y chromosome plays a role in cancer.

The Y chromosome has a small number of genes, and its primary function is to determine sex. Some dissed the Y as a “functional wasteland,” others called it a “nonrecombining desert.”

Last month, a team at Cedars-Sinai Samuel Oschin Cancer Center published a fundamental biological finding: the Y chromosome has an additional function. The loss of the Y chromosome makes cancer worse, and it does so by boosting the tumor’s ability to evade the immune system, they reported.

The study, published June 20 in Nature, is the first to suggest that:

- The Y chromosome drives cancer biology,
- The Y chromosome regulates cancer cells’ ability to interact with the adaptive immune system,
- Tumors with low Y chromosome expression are more vulnerable to checkpoint inhibitors,
- Loss of the Y chromosome might be a biomarker of cancer aggressiveness and immunotherapy response.

This finding may alter biology textbooks and may result in strategies for development of cancer therapeutic agents. The team, led by Dan Theodorescu, director of the Samuel Oschin Cancer Center, reported that the loss of the Y chromosome likely has near-term translational potential as a biomarker for predicting either tumor aggressiveness or immunotherapy response.

“I have to say, it has been quite an amazing journey,” Theodorescu said to The Cancer Letter. “The Y chromosome went from [being] very poorly studied—nobody was paying attention to it—to emerging in the past few years as being an important marker of developing cancer, and now with our work, a major driver of cancer aggressiveness.”

Preliminary data suggest that loss of Y chromosome is also of relevance to prostate cancers as well as other cancers, Theodorescu said to The Cancer Letter.

For the last five years, an epidemiological phenomenon pulled at Theodorescu’s mind: the Y chromosome is progressively lost in men as they age—loss of the Y chromosome, or LOY, in blood leukocytes is a prominent genetic alteration in human males, Theodorescu said to The Cancer Letter.

This loss is associated with some of the top causes of death in high-income countries: cancer, heart disease, and neurological disease.

“How can you have a chromosome that purportedly determines biological sex, but nothing else?” Theodorescu said. “If that is the case, why is it lost proportionally with age and associated with major human diseases? This does not add up.”

These two ideas didn’t click for Theodorescu. In his mind, there had to be more to the story.

Is LOY simply a biomarker of some underlying phenomenon, or is it more interesting than that? Does LOY actually cause these diseases, or make them worse?

His experiments suggest the latter, he said.

When Theodorescu started his career in the mid-nineties, most researchers did not consider biological sex as a relevant variable, particularly in mouse studies. In bladder cancer research specifically, the rationale at the time was that men...
have higher incidence than women due to higher smoking rates, so, it wasn't necessary to consider sex as a biological variable. That led to disregard for sex appropriate experiments.

Now, the NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies. Consideration of both sexes in experiments allows for sex-based comparisons and may inform clinical interventions.

Theodorescu said he hopes that his Nature paper will provide additional evidence for people to consider biological sex—and gender—when designing bench to bedside research projects.

The Cedars-Sinai catchment area includes the second largest LGBTQ+ population in the U.S., and the institution hosted the first national LGBTQ+ cancer symposium. The institution plans to repeat this symposium every other year.

"I want to emphasize the importance of awareness to sex and gender across the entire spectrum of cancer research and care," Theodorescu said. "We need to really consider this interplay between the chromosomes and the hormonal microenvironment in cancer and other diseases.

"I'm sure that this increased vigilance and awareness will provide major novel insights in cancer that will greatly benefit all patients."

The paper by Theodorescu et al. suggests important follow-up research questions relevant to transgender patients—notably, does loss of the Y chromosome have the same implications in bladder cancer for transgender women? His lab is currently investigating this, and other labs at Cedars-Sinai are studying questions aimed at helping transgender patients as well, such as defining transcriptional signatures of breast tissue from transgender men following androgen therapy.

"I'm optimistic about further studying the Y chromosome genes in cancer because we have already identified some promising therapeutic leads," Theodorescu said. "We certainly have many more experiments to do, but I can't help but be very excited about the results we have, as potentially something that could be helpful to our patients."

Theodorescu spoke with Jacquelyn Cobb, reporter with The Cancer Letter.

Jacquelyn Cobb: Dr. Theodorescu, congratulations on your recent Nature publication. It seems that something fundamentally important is happening.

Correct me if I'm wrong, but this is the first-ever demonstration that the Y chromosome has any role in cancer, and that the Y chromosome regulates cancer cell's ability to interact with the adaptive immune system.

Dan Theodorescu: Well, first of all, thank you very much for your interest in discussing our findings.

Yes, you're correct. Prior studies on the loss of the Y chromosome, or, as we like to call it, LOY, have focused on assessing the fraction of cells that have lost the Y chromosome in normal blood and in primary tumors.

But no one, as far as I know, has shown that Y chromosome loss can actually drive any cancer phenotype until our study. So, what our study shows is that loss of the Y chromosome can drive cancer aggressiveness in experimental models, and it turns out it can also be associated with poor patient prognosis in bladder cancer.

We also have preliminary data, unpublished, that LOY is associated with poor prognosis in other cancers. So, we're looking at that further using other experimental systems.

Is this also the first ever demonstration that low Y chromosome expression is associated with enhanced responses to immune checkpoint blockade?

DT: Yes, it is.

It was one of the most interesting and frankly, surprising, findings of our study—that loss of Y makes male cancer cells, and tumors resulting from those cancer cells, more aggressive. [Also surprising was] that, in fact, the reason for that increased aggressiveness was that the cancers were able to evade the T-cell dependent immune system.

The way the tumors that have lost the Y were doing this, is by causing T-cell exhaustion. T-cell exhaustion is—it's a state of the T-cell that ranges basically from complete lack of its effector function to altered functionality of the T-cell.

The bottom line seems to be that the loss of Y in the cancer reduces the destruction of the cancer, or the cancer cell, by the host immune cells, in this case, T cells.

This results in the tumors growing more aggressively and to larger sizes.

The way I read the paper, it suggests that loss of the Y chromosome might be a biomarker of cancer aggressiveness and immunotherapy response.

DT: This is a multiple part question. So, let me see if I can break this up a bit.
First of all, prior papers by others have very elegantly and thoroughly shown that loss of Y in peripheral blood cells is perhaps one of the most common, if not the most common, form of genetic alteration in men, and it occurs in nearly 20% of 80-year-old men.

These men have lost the entire Y chromosome in more than 10% of their blood cells. That’s the criteria for considering what we also call mosaic LOY, or mLOY.

It was one of the most interesting and frankly, surprising, findings of our study—that loss of Y makes male cancer cells, and tumors resulting from those cancer cells, more aggressive.

In addition to that, what was striking from this prior work was that these men that have mosaic LOY have an overall shorter survival, and that shorter survival was attributed to higher risks of cancer, higher risk of heart disease, and of neurological disease.

So, that is a fascinating connection. You could think of the Y chromosome loss, as being, if you will, a common thread among three major causes of death in men.

That’s fascinating because these diseases, on the surface, are not related, but we know scientifically that there are potentially many mechanisms that could be shared across these. And it really excites me a great deal to think about these commonalities of pathogenesis, especially if we can attribute them in part to a chromosome.

More recently, several papers, including our own, have shown that loss of the Y chromosome is associated with a more aggressive cancer phenotype. Our paper has significantly contributed to this field by being the first demonstration that in addition to this association, the loss of Y is actually a driver of more aggressive cancer.

So, in addition to being a biomarker, LOY in tumors appears in fact, to be a driver of cancer aggressiveness.

Speaking of biomarkers—we have shown in our paper is that loss of Y is a biomarker for response to checkpoint inhibitors.

As is the case for tumor growth and aggressiveness, LOY is also a driver of response to checkpoint inhibitors such as PD-1 and PD-L1. Those are the only ones we looked at, mechanistically in animal models and by association in human data sets.

I have to say, it has been quite an amazing journey, because the Y chromosome went from [being] very poorly studied—nobody was paying attention to it—to emerging in the past few years as being an important marker of developing cancer, and now with our work, a major driver of cancer aggressiveness.

So, the last comment I would like to make, in terms of its abilities as a biomarker, is the fact that looking and assessing the loss of the Y chromosome turns out to be actually quite easy.

It’s easy to do it on body fluids; it is easy to do it on tissues. So, I’m optimistic that we can actually develop clinical tests that may, if validated, guide the practice of precision oncology based on evidence of loss of the Y chromosome. Potentially, these could be relatively simple and relatively inexpensive.

That is absolutely fascinating. That’s a great segue, because I’m interested in talking about the clinical impact.

The paper hints at the possibility that tumors with loss of Y chromosome offer insight on novel avenues to prevent tumor immune evasion. Can you speak more to that?

DT: In research, there is never a dull moment. You discover things along the way. One of the things that we discovered, after we found out that loss of the Y chromosome is driving tumor growth and evasion to the immune system, is that this platform may offer a unique and novel ability to help discover other mechanisms of immune evasion beyond the ones that are known today.

We, in parallel to doing this paper, have embarked on a very serious effort to actually use this platform with the aim of identifying other potential mechanisms of immune evasion.

Of course, we’re hoping that some of the things that we will discover, may be able to be converted into therapeutic targets that could be eventually used in patients.

I’m optimistic about further studying the Y chromosome genes in cancer because we have already identified some promising therapeutic leads.
We certainly have many more experiments to do, but I can’t help but be very excited about the results we have, as potentially something that could be helpful to our patients.

We should know the biologic sex of our cell lines, of our animal models, and we should not use biologic female models of cells into anything but the appropriate biologic sex of whatever the experimental animal is.

I would strongly encourage this approach, because we know too much about these differences now. We should no longer do experiments that are not biologic sex appropriate. This point is slightly different than doing experiments in both biological sexes, it’s about matching, when appropriate, the cancer cells with the host recipient.

I’m suspecting, and I’m hoping, that it will be progressively more investigated in these roles in cancers of all types and in situations of all types and in treatments of all types.

If I can make one other comment regarding an aspect of cancer biology and cancer research that’s important—I think what this work and that of others, really highlights the importance of awareness of sex and gender in cancer research and how important that is and how we need to pay attention to it. Because not only will we discover new things, but we’ll do the right thing by our patients and move science forward.

Let me give you one practical example of how awareness of this could be relevant to experimental cancer research.

In my opinion, it’s not okay—knowing what we know now—to do experiments in tumors, that are clearly relevant to both biologic sexes, in experimental models that don’t follow that, if you will, biologically relevant models.

Having one or both of those genes be altered in some way—by mutation or by loss or by amplification, by multiple potential mechanisms—it is conceivable that some of these genes may play a role in cancer biology and also response of the cancer to immunotherapy in women. In fact some of these genes have shown to be involved in the aggressiveness of bladder cancer.

So, apart from a couple of examples on the X chromosome that are important in bladder cancer growth, for example, there’s I think a real lack and a real need to study the X chromosome in both biological males and biological females, with all the advanced molecular biology tools that we have, to really get a very good understanding of what role these genes have in both men and women.

That’s wonderful. Like you just mentioned, considering gender and biological sex in cancer research studies, this paper really is about bladder cancer in patients assigned male at birth, people with a Y chromosome. Are there any implications from the study for women or for transgender patients?

DT: Well, that’s a very interesting question you ask. We have a significant interest in this because many genes on the Y chromosome have what are called paralogs that are on the X chromosome, and those paralogs and their importance, first of all, in the context of the Y chromosome genes have not really been studied.

So I suspect—and we’re doing these experiments now—that the role of those paralogs and their importance in cancer biology will very much depend on the presence or absence of the Y chromosome.

Similarly, if you think of these paralogs in women that have two X chromosomes, and you think about potentially having one or both of those genes be altered in some way—by mutation or by loss or by amplification, by multiple potential mechanisms—it is conceivable that some of these genes may play a role in cancer biology and also response of the cancer to immunotherapy in women. In fact some of these genes have shown to be involved in the aggressiveness of bladder cancer.

Absolutely.

I’d love to hear how you got here, how you became interested in this topic, and how you arrived at these findings. What originally inspired you to research the relationship between the Y chromosome and bladder cancer, and were you surprised by anything?

DT: We got into this primarily through our work, many years ago, on looking at the role of androgen in bladder cancer.

Androgen is something that is very critical to prostate cancer growth, but we, and others, have shown that it is important in bladder cancer as well.

That got me thinking more and more about the issues surrounding biologic sex in bladder cancer. One thing led to another, and since men have a bigger bladder cancer burden than women, and the two primary determinants of biologic sex are hormones and chro-
mosomes, we began working on the Y chromosome.

So, that’s how we got into it. Of course, I was very intrigued by the loss of the Y chromosome in blood. Those papers have been around for some time, and they’re quite intriguing, especially their relationship with increased risk of cancer.

The other point was that I was quite intrigued by the relationship with other diseases as well, because we know, more and more, that there are links between, for example, obesity and cancer, obesity and heart disease.

So, the fact that the Y chromosome seemed to also be a tie between some of these diseases got me even more interested.

One other thing that I forgot to mention got me interested in LOY was that because bladder cancer is a tobacco-related cancer... and it turns out that smoking has been associated with loss of the Y chromosome in the blood. So, there are three big reasons why we are really interested in the Y chromosome loss and why we used bladder cancer to test our hypotheses, and like they say, the rest is history.

That is so fascinating. I can’t wait to see more work that comes out of your lab.

Is there anything that we missed?

DT: I don’t think there’s anything else, except, I want to emphasize the importance of awareness to sex and gender across the entire spectrum of cancer research and care. We need to really consider this interplay between the chromosomes and the hormonal microenvironment in cancer and other diseases.

I’m sure that this increased vigilance and awareness will provide major novel insights in cancer that will greatly benefit all patients.

Thank you so much.

““
I want to emphasize the importance of awareness to sex and gender across the entire spectrum of cancer research and care. We need to really consider this interplay between the chromosomes and the hormonal microenvironment in cancer and other diseases.

“"
As researchers consider using circulating tumor DNA as an endpoint in clinical trials to evaluate drug efficacy, a collaboration led by Friends of Cancer Research is creating the evidentiary roadmap for the use of ctDNA in regulatory decisions.

As tumor cells die, small pieces of DNA are released into the bloodstream, and detectable levels of ctDNA can be used as a novel prognostic indicator of response to a therapeutic regimen, and potentially as an intermediate endpoint that is predictive of survival outcomes. These research questions are the focus of the multiphase collaboration between Friends, FDA, NCI, clinical researchers, pharmaceutical companies, and diagnostics companies.

The initiative, ctDNA for Monitoring Treatment Response (ctMoniTR) Project, is designed to examine these associations, and provide openly accessible information that would be useful for trialists looking to investigate the utility of ctDNA levels as an endpoint in prospective studies.

The ctMoniTR project seeks to address a specific question: Do changes in ctDNA levels reflect a patient’s response to treatment?

Based on retrospective analyses of data aggregated from clinical trials, the answer is “Yes”—thus far, for non-small cell lung cancer patients treated with...
PD-1/L1 checkpoint inhibitors, and now, based on new ctMoniTR data, with tyrosine kinase inhibitors.

“When looking at patients who have detectable ctDNA prior to therapy, patients for whom ctDNA remains detectable following therapy, those are the ones that fare worse and don’t seem to be responding as well in terms of long-term outcomes,” Jeff Allen, president and CEO of Friends of Cancer Research, said to The Cancer Letter. “But for patients for whom ctDNA is no longer detectable, those show improved outcomes. Interestingly, that change in ctDNA associated with better outcomes was measured within the first 10 weeks following treatment.”

Friends will be convening a meeting July 11 at Washington Marriott Georgetown in Washington, DC, to present key initial results and discuss the implications of these findings for clinicians and regulators. Richard Pazdur, director of the FDA Oncology Center of Excellence, will be presenting the lunch keynote address.

The registration form is available on the Friends website.

“We will be showing next week that at these early time points, the change of ctDNA to be no longer detectable within the first 10 weeks is associated with improved long-term benefit (PFS and OS). We also looked at whether data from the first RECIST evaluation was an indicator of outcomes—and the ctDNA change was a better indicator of long-term benefit than the first RECIST evaluation was,” Allen said. “When looking at imaging results at a similar early timepoint, grouping those as responders and non-responders by radiographic imaging wasn’t actually an indicator of long-term outcomes. But the change in ctDNA was. It really could be a very useful tool.

“I think the meeting will be a great opportunity to really dive deep into the results. There will also be data from a Baseline ctDNA Project as well as the ctMoniTR Step 2 project that haven’t been presented before,” Allen said. “We’ll have various experts that were involved in and guiding these studies that will be describing the results and thinking about what the next steps should be, including participants from the FDA.”

If these findings are replicated and validated in prospective clinical trials across different disease and therapeutic settings, it is likely that FDA would consider approving drugs with ctDNA as an early endpoint, which could allow a potentially efficacious product to enter the market before confirmatory survival data is obtained.

“ctDNA could be used in early phase clinical trials to aid in signal finding of drug activity and to potentially aid sponsors in their drug development plans,” the agency wrote in a draft guidance published May 2022. “FDA encourages sponsors to develop evidence regarding the usefulness of ctDNA response in addition to or supporting pathologic complete response information after neoadjuvant therapy.”

A series of retrospective studies

The ctMoniTR collaboration, now in its fifth year, is in the “Step 2” phase of the project, which aims to study the association between decreases in ctDNA levels with improved survival outcomes across multiple therapeutic areas and classes of drugs:

- **Module 1**: Advanced NS-CLC with TKI
- **Module 2**: aNSCLC with anti-PD(L)1 and/or chemotherapy
- **Module 3**: Solid tumors, including melanoma, breast, head and neck, ovarian, and colorectal, with anti-PD(L)1 or TKI

- Cross-module analysis: Combine data from all modules

The Step 2 Module 1 findings, which were derived from a retrospective aggregate analysis of eight clinical trials of patients with aNSCLC treated with a TKI (i.e., anti-EGFR, ALK, RET, or MET; n=1590), were presented as a poster at the annual meeting of the American Society of Clinical Oncology in early June.

“Patients who had detectable ctDNA levels prior to therapy and then following treatment, if those detectable levels of ctDNA were no longer detectable—so, the ctDNA levels were depleted by therapy—those patients had better outcomes in both progression-free survival and overall survival,” Allen said.

The authors of the TKI study also concluded that ctDNA samples collected within 10 weeks following initial treatment can be used to assess response to treatment and are an indicator of long-term benefit.

In Module 2, the project will include multiple studies with comparator arms evaluating chemotherapy vs. immunotherapy and will be useful to determine whether differences can be predicted based on treatment type.

“We have an impressive statistical operation that is really the foundation of this entire project,” Allen said. “Cancer Research And Biostatistics, or CRAB, serves as the independent analysis center for the project. The NMD Group, led by Névine Zariffa, is a key statistical advisor that we have, and our statistical working group comprised of experts from the data partners and FDA meets biweekly and has been critical for designing the protocol, setting the statistical analysis plan, and evaluating
ongoing analyses. This has been a true partnership, and we're very appreciative of all that have been involved."

The TKI study builds on the project's Step 1 findings, which were published August 2022 in *JCO Precision Oncology*. In Step 1, the investigators observed strong associations between reductions in ctDNA levels from on-treatment liquid biopsies with improved OS (HR, 2.28; p < 0.001) and PFS (HR, 1.76; p < 0.001) in a pooled analysis of five independent clinical trials with NSCLC patients who were treated with immune checkpoint inhibitors.

"Even with the level of variability across different diagnostic assays, and even variability that came with different sampling time points as an example, we were still able to see these strong associations with reduction in ctDNA and improvement in overall survival," Allen said. "[The Step 1 results] really served as the prototype here showing that 1) these types of data could be aggregated through this unique partnerships, and 2) that ctDNA change may be a biomarker that could be an indicator of response to therapy and has potential to accelerate drug development, and actually be a tool that can help inform regulatory decision making into the future."

**A novel prognostic indicator and endpoint**

Beyond drug development, ctDNA has become an important biomarker in routine clinical care for patients with metastatic NSCLC.

In November 2022, results from a large prospective cohort study published in *Nature Medicine* provided confirmation of the clinical utility of ctDNA in treatment decision-making—demonstrating that patients who were matched to targeted therapy by ctDNA sequencing experienced a nearly 40% reduction in mortality, based on an adjusted multivariate analysis that included disease stage, targeted therapy, tumor volume, and even metabolic tumor volume (*The Cancer Letter*, Nov. 18, 2022).

Although patients with advanced stages of disease are more likely to shed ctDNA, which is associated with a poor prognosis, there is variability by tumor stage and type.

"In advanced disease, tumor types such as colorectal cancer are positive for ctDNA presence in almost 100% of the cases, whereas this is the case in ~75% of patients with NSCLC or breast cancer," Ana Vivancos and Josep Tabernero, of the Vall d’Hebron Institute of Oncology, wrote in a companion piece to the Jee et al. paper.

Patients who had detectable ctDNA levels prior to therapy and then following treatment, if those detectable levels of ctDNA were no longer detectable—so, the ctDNA levels were depleted by therapy—those patients had better outcomes in both progression-free survival and overall survival.

— Jeff Allen

"In contrast, only ~30% of patients with metastatic gastrointestinal stromal tumors show detectable ctDNA in plasma."

These considerations, particularly whether decreasing ctDNA levels on treatment are predictive of response and survival in other cancer types, would need to be explored in greater detail as the ctMoniTR project moves into studying the utility of ctDNA in other solid tumors beyond NSCLC in Module 3.

The upcoming July 11 meeting will also delve into results of the Baseline ctDNA Project that examines pre-treatment ctDNA levels across different major tumor types and stages, as well as explore potential differences between numerous assays.

"The Baseline ctDNA research partnership involves eight different assays and test developers. We'll be presenting information from five different tumor types," Allen said. "These data will show that late-stage tumors produce more ctDNA at a more detectable level. And in looking at those late-stage cancers, at least the five cancers that we've looked at initially, we've seen that there's been similar detectability and similar ability to measure ctDNA across those different tumor types.

"So, while the initial ctMoniTR data is in lung cancer, the Baseline Project reinforces that ctDNA can be valuable in a number of different tumor types, which really could help us begin to understand its utility across the entire cancer research continuum," Allen said. "I think some of that will really build on the baseline work to understand the kinetics across numerous different tumor types, how similar or not they actually are. And so, the Baseline project was a useful exercise to begin to understand how different some of these measurements were across late-stage tumor types."

FDA will be paying particular attention to the limitations of these studies as the
agency evaluates the evidence that is generated in the ctMoniTR collaboration.

“I think what regulators will likely want to see moving forward are prospective studies that select the thresholds in advance, in order to not have potentially biased results, to be able to help better understand those outcomes in a prospective manner,” Allen said. “I hope what we’re able to provide by going through the ctMoniTR process is begin to establish some of those methodologies and explore some of those potential thresholds and other study attributes for which a prospective trial could be designed.”

A threshold that needs to be examined in the future, for example, pertains to the magnitude of change in ctDNA level, and at which cutof f points would those changes be considered to be clinically meaningful.

“What we looked at here was a percent change from baseline,” Allen said. “So, we were able to normalize the variability between the different assays. The different assays that were used do have different characteristics, a different limit of detection as an example, or they may have different sensitivity or specificity, so we needed a common metric in order to be able to combine data from multiple trials.

“So, each patient always received the same test, even if each trial did not necessarily utilize the same tests across the multiple different trials in that cohort, but by looking at a percent change of variant allele frequency, we’re able to normalize those values.”

More studies are needed before ctDNA response rates can be reliably used as a regulatory endpoint, but for now, there is sufficient evidence to support the use of ctDNA as a selection criterion.

“By selecting patients who had detectable levels of ctDNA at the outset of a trial, you could construct a clinical trial that would go a little bit faster, at least for obtaining an initial indicator of drug activity,” Allen said. “Ultimately, when that evidence does get brought before the regulators, hopefully they’ve had the opportunity to have access to this information and ask questions of the data along the way, to help inform the questions that they may ask as the prospective trials are being designed.

“I hope that we are providing robust evidence that is beginning to show that ctDNA change is a viable biomarker for evaluating potential treatment efficacy.”

Even with the level of variability across different diagnostic assays, and even variability that came with different sampling time points as an example, we were still able to see these strong associations with reduction in ctDNA and improvement in overall survival.

— Jeff Allen
Threats to the NCI COE agenda impede our ability to meet the needs of our cancer center catchment area communities

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Community Outreach and Engagement (COE), now augmented with the Plan to Enhance Diversity (PED), is critical and central to the impact of NCI-designated cancer centers, and both are set forth as required components for the NCI Cancer Center Support Grant (CCSG).

As COE leaders, we embrace the NCI’s increasing prioritization of these components. However, emerging legislative actions and social forces outside of the control of NCI-designated Cancer Centers completely threaten substantive efforts to achieve equity in cancer prevention, control and care; and severely hinder centers’ capacity to eliminate persistent racial/ethnic disparities in cancer outcomes.

The NCI’s COE initiative has evolved tremendously over the past decade. Prior to 2010, the initiative only existed secondarily as community engagement activities required to differentiate NCI-Designated Cancer Centers from NCI Comprehensive Cancer Centers.

By 2012, the guidelines for what would become COE changed to require a concerted effort to ensure that the Centers were deeply engaged with the communities and patients they serve and that the research conducted was both relevant and impactful to each center’s defined catchment area.

Over time, COE has emerged as an urgent imperative to address longstanding cancer disparities. The imperative of COE is underpinned by advances in the science of health disparities and community engagement, accelerated by the increasingly visible killings of unarmed Black and brown people, and the heightened public awareness of health disparities which became painfully apparent during the COVID-19 pandemic.

In 2021, PED also was introduced as a new, required component of all centers competing for NCI support and comprehensive cancer center status.

As part of the elevated prominence of COE and the associated urgency to address issues of health equity and diversity, an increasing number of scientific meetings have emerged.

These meetings provide opportunities for community engagement leaders to hear from their colleagues at other centers, share best practices and strategies for delivering on the promise of COE, refine metrics, and prepare for respective site visits. Because most of these meetings are not officially sponsored by the NCI, they are held in the state of the host institution on a voluntary basis.

The past few years in the US have been extraordinary with respect to the challenges facing our democracy. Some states are undergoing a surge in legislation that re-restricts voting rights, largely targeting communities of color.

Other laws serve to ban or remove selected books about U.S. race relations, and sexual orientation from school libraries; limit discussions of U.S. history, including slavery; prohibit the teaching of Advanced Placement African American history courses; eliminate diversity, equity and inclusion activities in publicly funded institutions, restrict discussions about and support for LGBTQIA communities, including punishment for the use of terminology related to its members; and restrict access to both gender affirming care and maternal child health care.

In response to legislation that limits the freedoms of traditionally marginalized communities, the country’s largest LGBTQIA advocacy groups and the NAACP have issued travel advisories for the state of Florida.

In a press release dated May 20, 2023, the NAACP states: “Florida is openly hostile toward African Americans, people of color and LGBTQ+ individuals. Before traveling to Florida, please understand that the state of Florida devalues and marginalizes the contributions of, and the challenges faced by African Americans and other communities of color.”

While no such advisory has yet been issued for other states, Texas has taken a similar approach to reducing personal freedoms that disproportionately impact women, racial/ethnic marginalized populations and people who identify as part of the LGBTQIA community.

The 2023 Cancer Center Community Impact Forum (CCIF) will be held in Florida by the host institution, Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine.

The state taxes paid through hotel fees and other conference expenses will continue to empower and strengthen policies of hate and discrimination. An immediate reaction, which would be an appropriate one, would be to protest convening these meetings in states with policies that disenfranchise segments of the population.

However, it is critical to acknowledge that important conversations about the politics and policies of hate need to take place, especially in the states that have operationalized such policies.

Therefore, COE meetings in these states may provide unique opportunities to confront and create strategies to counter these policies and reaffirm our collaborative commitment to advance COE.
Health equity requires intentional action.

Therefore, hosting these important conversations will require a departure from business as usual. We strongly encourage coordination between the NCI and cancer centers when planning events and meetings so that we don’t hurt or undermine our colleagues and program leaders at NCI with potential boycotts or low turnout.

In addition, we have several recommendations that demonstrate a commitment to goals of COE and PED.

First, the COE meetings must be organized, led and prominently feature training and perspectives from minoritized and marginalized populations who are under attack. Unfortunately, at many COE meetings, these populations are not given the platform to speak their truth. Their voices are rarely heard directly, and their perspectives are rarely centered.

Second, the meeting objectives must set the stage by addressing the current, pending, and planned legislation consistent with non-inclusive policies and the potential impact on COE initiatives. The objectives should also include the development of a plan to challenge policies of hate against marginalized and minoritized populations that directly undermine COE efforts.

Third, meetings should incorporate a dedicated session that focuses on specific strategies cancer centers can employ to counter and address the state policies of hate and discrimination. The most impactful meeting outcomes will also include a position paper or other publication firmly challenging discriminatory policies impeding COE progress.

Finally, a strong statement from the NCI and cancer center directors about the potential harms of laws which deny the very existence and history of the marginalized communities COE programs are intended to engage and serve is much needed. This statement would provide critical guidance about how the NCI and site visitors will hold cancer centers accountable for impacting their communities in regions where such staff and leaders are legally restricted from doing so.

In the absence of a substantive commitment to the rights of women, Black, brown and LGBTQIA+ community members to live freely, to be counted, and to have the burden of cancer in these populations addressed, COE and PED’s activities would be empty or performative at best.

In 2022, the Alliance of Black COE Scientific Directors comprised of deputy/associate directors from several NCI-designated Cancer Centers was formed to develop strategies to effectively address the NCI CCSG COE agenda.

The primary goal of the alliance is to share best practices on community outreach and engagement, learn from each other and work collectively to impact the cancer burden within our respective center’s catchment areas.

As Black people, it is unclear whether going to meetings that take place in settings the NAACP describes as ‘openly hostile toward African Americans, people of color and LGBTQ+ individuals,’ is worth putting our values and perhaps even our lives at risk.

Participation would ironically be advancing an agenda that marginalizes and minimizes us and the communities from which the alliance members come.

Nonetheless, we remain committed to the diverse residents in our respective catchment areas, fighting for their voices to be heard and their needs to be met, reducing the burden of cancer and eliminating longstanding cancer disparities.

As the Alliance of Black COE Scientific Directors, we are calling on all of our allies to join us in pushing back against the policies of hate sweeping across our nation and impeding our ability to achieve the ideals put forth in the NCI guidelines for PED and COE.

Written on behalf of The Alliance of Black COE Scientific Directors
Susan Love, a transformative leader in breast cancer movement, dies at 75

She intuitively understood the right thing to do—and then just did it

By Frances M. Visco, JD
In May 1991, I sat in a law firm conference room in Washington, DC, listening to a pitch from a small group of women who had the idea to launch a political advocacy movement around breast cancer. One of those women was Dr. Susan Love. The person next to me nudged me with her elbow and whispered, “She is famous. She wrote this unbelievable book.”

Though I had received a breast cancer diagnosis just four years earlier, I knew very little about the issue or the players—I just knew I wanted to do something about it. And it was very clear to me that day that Susan Love had the vision and the balls to make something big happen.

That was my introduction to Sue, and what was to become the National Breast Cancer Coalition (NBCC). For more than 30 years, I had the privilege of working with Susan to grow NBCC into a strong, powerful movement. But in May 1991, no one knew who NBCC was. The fact that Dr. Susan Love was part of NBCC’s launch gave it credibility among many and instilled fear in some.

Susan died of recurrent leukemia on July 2. She was 75.

Susan was never one to pull punches. She was fearless. Breast cancer revolved around mammography at the time, not so different from today. Sue questioned that and taught us to do the same. As others celebrated the next chemotherapy drug or new radiation equipment, Sue would give her famous line: It’s all still “slash, burn, and poison.” And that allowed patients to question the traditional treatments and wonder why it wasn’t changing.

Susan demystified breast cancer for the public in speeches, articles, media appearances, and most importantly through “Dr. Susan Love’s Breast Book,” the bible for women diagnosed with breast cancer. I have heard many women say they fell asleep clutching that book, after poring through it all day.

Susan knew women could absorb complex information about breast cancer—and she knew that they craved it. She gave them what they wanted and needed: the power of knowledge to understand what was happening to them, to know the right questions to ask their doctors, and to know they had every right to do so. Susan helped lead NBCC advocates into the world of science, as collaborators, with a meaningful seat at the table.

Sue had many innovative ideas—some of them pretty wild—and she never hesitated to act on them. She had the guts to say things others would not.

Early on, Sue pointed out the lack of evidence behind hormone replacement therapy and expressed concern about its safety, and that it might increase breast cancer risk. She was attacked over that. In fact, I clearly recall seeing an issue of The New Yorker with a cover flap touting an article asking “how wrong is Dr. Susan Love?”

Except she wasn’t wrong. Not long after, evidence was published supporting her position. Susan Love was, in fact, right. (This wasn’t always the case, of course. She was too innovative to be right all the time. And when she wasn’t right, she would smile, shrug, and move on to the next incredible thing.)

After the publication of the first edition of “The Breast Book,” Sue spoke to a group of, in her words, “older” women in Salt Lake City. She felt her speech was going on too long and was a bit ponderous, so to lighten things up, she suggested they all go to DC and march topless to the White House demanding attention to breast cancer. Sue waited for the laugh, but what she got was a resounding “Sign us up!”

She said she knew at that moment it was time to organize and get political. At the same time, Susan Hester, the founder of the Mautner Project for Lesbians with Cancer, was thinking the same thing. Together, they reached out...
The Faulkner Breast Center was one of the first NBCC groups, and when she launched the Susan Love Breast Cancer Foundation, that organization joined NBCC’s board.

Susan’s network of doctors and researchers, most outside the traditional thought-leader groups, came along with us when she asked, because she asked. As NBCC developed a plan for the research needed to support our “$300 Million More” campaign that led to the creation of the DOD BCRP, Sue pulled in her network to help us develop it.

When she and I attended a science workshop by a large professional association, I vividly recall Susan and I sitting around during a break, planning our own meeting, so we could question the traditional approach we were hearing.

That led to the NBCC’s Aspen Project think tank meetings, which led to The Artemis Project, which led to the development of a preventive vaccine that will soon begin a phase I trial. Susan was there for all of it.

She was serious about ending breast cancer, but didn’t take herself seriously. Sue was irreverent, funny, and fun. In the introduction to the second edition of “The Breast Book,” she discussed how much had changed, and described having to add chapters and edit all but one, the first on anatomy—“The breast, I’m glad to report, is still located on the chest!”

When NBCC started holding advocacy conferences in Washington, DC, for members from across the country, Susan said we had to celebrate ourselves. And so, we hired a DJ, and on the final night of the meeting each year, Susan would lead us onto the dance floor, where we would all wildly dance.

She loved fine wine, dancing, meeting people, and helping others. She was a techie, an early adopter, and very early on, with advocate Pat Barr, pushed NBCC to get on board with email, which most of us thought would never catch on. Ok, so once again, Susan Love was right. She’s smiling.

One of NBCC’s longtime advocates used to work with Susan at the Faulkner Breast Center, which Susan founded. She told me when Sue came back from that May meeting, she had a huge smile and said, “We are going to end breast cancer for the future, and I think you are going to want to come aboard.”

NBCC likely would not exist if it were not for Sue Love.

She spoke to thousands of women everywhere, giving them the courage to help themselves and others. And she would always tell her audience to become part of the movement. Over the years, Susan remained loyal to NBCC.

The Faulkner Breast Center speaking at a 1993 White House event with Bill and Hillary Clinton where the National Breast Cancer Coalition delivered 2.6 million signatures asking for a National Action Plan on Breast Cancer.
she told me she had to run, because she was meeting with NASA about yet another idea.

When many lamented the fact that not enough women were enrolling in research studies, Susan created the Army of Women (now Love Research Army), so people could sign up to do just that. After an appearance on Good Morning America, almost 300,000 people said yes.

It is rare, but there are times some of us are lucky enough to know and work with an individual who is transformative. Someone who intuitively understands the right thing to do and then just does it. That certainly was Susan.

Research, policy, healthcare, activism... it all changed in breast cancer in response to her initial vision.

These past few days, I have been going back over my past emails from Susan. I could never publish some of them, but sure wish I could. In one of her more recent messages to me, not long after she learned her leukemia had recurred, she spoke about her work with NBCC and ended with this:

“We have certainly had a great run.”

Without Sue, we would still be crawling. Thank you, my friend.

Frances M. Visco, JD, is the President of the National Breast Cancer Coalition.
When Susan Love joked that a group of breast cancer advocates in Salt Lake City should march topless to George H. W. Bush’s White House, she didn’t expect to be taken seriously.

“When we said, ‘We should march topless on the White House,’ they were ready,” Love, founder and chief visionary officer of the Dr. Susan Love Foundation for Breast Cancer Research, said to The Cancer Letter. “The idea of all these topless women marching on the White House was enough to launch the breast cancer advocacy movement.”

It was June of 1990, just after Love published her book, “Dr. Susan Love’s Breast Book,” which walks its readers through the radical changes in the science of breast cancer at the time. She was on a book tour that landed her in Salt Lake City, where around 600 people showed up to hear her speak.

“What I really learned when we were at this meeting in Salt Lake City, is if you have the right answer at the right time, people are ready. They were ready to do something,” she said. “It was a time when we had science, and we had the NSABP doing research and randomized trials, and we could start to change how we treated breast cancer based on data, which was really something new and novel.”

The science and the culture of breast cancer activism was changing.

“We had a randomized controlled trial comparing wide excision or lumpectomy and radiation, to mastectomy. The fact that women were willing to be randomized as to which they got, by itself, was pretty remarkable,” Love said. “It turned out that lumpectomy or wide excision, followed by radiation, was just as good as mastectomy, much to everybody’s amazement.”

Breast cancer advocacy of earlier years—marked by building awareness, something critics called “pinkwashing”—was less political and not nearly as confrontational, Love said.

The AIDS activists had inspired a new kind of activism, and breast cancer activists took note. The National Breast Cancer Coalition, an umbrella group that revolutionized the goals and tactics of cancer patient advocacy, was emerging, Love said.

“This was, ‘We want to be at the table. We want to be making the suggestions and making sure they happen, not just marching around wearing pink,’” she said. Also, most of these activists were not physicians or scientists, or involved in treating or studying breast cancer at all.

“They were regular people who had had breast cancer, or their mother had had it, or their sister had had it, and they were eager to hear the science and they were eager to look to how we could end it,” she said.

Women didn’t know that much about breast cancer, and we wanted them to be able to represent what was going on,” Love said. “We started educating them in a program called Project LEAD, and we got different scientists to come, and over a weekend, we would educate them on breast cancer.”
• Breast surgeon and advocate Susan Love weds surgeon Helen Cooksey in San Francisco
By Cancer History Project | Feb. 20, 2004

Susan Love, NCAB member, author, and a founder of the breast cancer advocacy movement, wed her partner of 21 years Helen Sperry Cooksey in San Francisco on Feb. 15, four days after San Francisco Mayor Gavin Newsom directed the city to legally marry same-sex couples.

Cooksey, a general surgeon at the Jeffrey Goodman Clinic of the Gay and Lesbian Center in Los Angeles, Love, and their 15-year-old daughter Katie stood outside City Hall for eight hours last Sunday with hundreds of other couples.

Late in the afternoon, Love and Cooksey were married under the Rotunda with Katie as witness and Michael Farrah Jr., senior advisor to the mayor, officiating. “I don’t know what the courts will do, but it sure felt like a Rosa Parks moment,” Love said. “It is important for gay people to be able to get married and we sure are happy to have the opportunity.” The family lives in Pacific Palisades, CA.

• Podcast: 50th Anniversary of the Johns Hopkins Kimmel Cancer Center Podcast Series—Oncology Nursing
By Johns Hopkins Kimmel Cancer Center | July 5, 2023

Bill Nelson, director of the Johns Hopkins Kimmel Cancer Center, speaks with Donna Berizzi, senior director of oncology nursing at Johns Hopkins, about the past, present and future of oncology nursing.

This column features the latest posts to the Cancer History Project by our growing list of contributors.

The Cancer History Project is a free, web-based, collaborative resource intended to mark the 50th anniversary of the National Cancer Act and designed to continue in perpetuity. The objective is to assemble a robust collection of historical documents and make them freely available.

Access to the Cancer History Project is open to the public at CancerHistoryProject.com. You can also follow us on Twitter at @CancerHistProj, or follow our podcast.

Is your institution a contributor to the Cancer History Project? Eligible institutions include cancer centers, advocacy groups, professional societies, pharmaceutical companies, and key organizations in oncology.

To apply to become a contributor, please contact admin@cancerhistoryproject.com.

IN BRIEF

David W. Craig named founding chair of Department of Integrative Translational Sciences at City of Hope

David W. Craig was named professor and inaugural founding chair of Department of Integrative Translational Sciences within Beckman Research Institute of City of Hope. Craig was also named deputy director of translational sciences at Beckman Research Institute.
and associate director of data science for City of Hope’s NCI-designated comprehensive cancer center in Los Angeles.

The Department of Integrative Translational Sciences will focus on precision measurement, data science, and diversity. It will seek to improve translational outcomes and the basic science of precision medicine.

Craig joins City of Hope from the University of Southern California, where he was co-director of the Institute of Translational Genomics and vice chair of the Department of Translational Genomics at Keck School of Medicine of USC. He was the director of the Norris Comprehensive Cancer Center Molecular Genomics Core and created their translational biomedical informatics master’s degree program.

Prior to USC, Craig served as the deputy director of bioinformatics at Translational Genomics Research Institute, was director of its Neurogenomics Division and co-founded a genome and whole exome sequencing laboratory that is now integral to City of Hope’s precision medicine program.

At City of Hope, Craig will lead the establishment of a transdisciplinary team of biologists and data scientists who will work with engineers, biologists, chemists, and clinicians across the system to enhance City of Hope’s patient-centered mission.

He also will collaborate with regulatory agencies, industry partners, researchers, and health care professionals to integrate scientific findings and translate potentially practice-changing discoveries into improved patient care and human health.

Over the past 15 years, Craig’s lab has developed experimental and computational tools that bridge engineering, biotechnology and clinical care interfaces. Craig has spearheaded collaborative computational and data science efforts within large and small research consortia, including the 1000 Genomes Project and the Bipolar Genome Study.

“I am eager to work with the exceptional leadership, faculty and staff at City of Hope to build upon our pioneering work in genomics and precision medicine. I look forward to translating unique insights from large datasets into actionable strategies in the clinic,” Craig said in a statement. “At City of Hope, we will continue to enhance our ability to work across departments to make data-driven decisions and, ultimately, advance City of Hope’s mission to build bridges that fast-track the development of lifesaving therapies.”

Crapo, Bennet, Cardin, and Scott introduce legislation to expand coverage of MCEDs

On June 22, Sens. Mike Crapo (R-ID), Michael Bennet (D-CO), Ben Cardin (D-MD), and Tim Scott (R-SC) introduced the Medicare Multi-Cancer Early Detection Screening Coverage Act, which would grant Medicare the authority to cover multi-cancer early detection tests once they are approved by FDA.

“As health care professionals, we continually work to integrate new technologies into prevention, detection, and treatment for our patients. Multi-cancer early detection screening harnesses the latest technology to catch cancer earlier, giving patients a greater chance at survival,” Barbara Schmidtman, chair of the ACCC Governmental Affairs Committee, said in a statement. “We are counting on Congress to pass the Medicare Multi-Cancer Early Detection Screening Act this year so all patients—especially older Americans—have access to these game-changing tools.”

For years, health care professionals have relied on early detection screenings for only five types of cancer. MCED tests give clinicians the ability to screen for dozens of types of cancers at once—many of which currently have no early detection methods. Because these tests require only a single draw of blood, they can be administered in a wide variety of health care settings.

Early cancer detection has been shown to improve outcomes for patients, enhance their quality of life, and lower treatment costs.
Datopotamab deruxtecan improves PFS in advanced NSCLC, phase III trial shows

Positive high-level results from the TROPION-Lung01 phase III trial showed datopotamab deruxtecan (Dato-DXd) demonstrated a statistically significant improvement for the dual primary endpoint of progression-free survival compared to docetaxel, the current standard of care chemotherapy, in patients with locally advanced or metastatic non-small cell lung cancer treated with at least one prior therapy.

For the dual primary endpoint of overall survival, the data were not mature, and the early trend observed in favor of datopotamab deruxtecan versus docetaxel did not meet the prespecified threshold for statistical significance at this interim analysis.

Datopotamab deruxtecan is a specifically engineered TROP2-directed DXd antibody drug conjugate being jointly developed by AstraZeneca and Daiichi Sankyo.

The trial will continue as planned to assess OS with greater maturity. The investigators and participants will remain blinded to the results, the companies said.

The safety profile of datopotamab deruxtecan was consistent with previous clinical trials with no new safety signals identified. All grade interstitial lung disease was generally consistent with prior clinical trials, with the majority being low grade. Some Grade 5 events were observed.

"With TROPION-Lung01, we met the dual primary endpoint of progression-free survival, challenging the entrenched standard of care in a previously treated and unselected patient population that has long deserved an alternative to chemotherapy," Susan Galbraith, executive vice president of oncology R&D at AstraZeneca, said in a statement. "These first phase III trial results from the datopotamab deruxtecan clinical programme provide compelling evidence for the potential role this TROP2-directed antibody drug conjugate can play in treating patients with lung cancer."

For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC in the absence of other treatment options and despite limited effectiveness and known side effects. TROP2 is a protein highly expressed in a large majority of lung cancers. There are currently no TROP2-directed ADCs approved for the treatment of patients with lung cancer.

"We are encouraged by the statistically significant results of the dual primary endpoint of progression-free survival seen with datopotamab deruxtecan and look forward to the final overall survival analysis," Ken Takeshita, global head of oncology R&D at Daiichi Sankyo, said in a statement. "We plan to share these data with regulatory authorities to discuss next steps."

TROPION-Lung01 enrolled patients with and without actionable genomic alterations, such as EGFR and ALK. Patients with actionable genomic alterations were previously treated with platinum-based chemotherapy and an approved targeted therapy. Patients without actionable genomic alterations were previously treated, concurrently or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

FDA grants priority review to zolbetuximab for gastroesophageal junction adenocarcinoma
FDA has accepted and the Biologics License Application for zolbetuximab, a first-in-class investigational Claudin 18.2-targeted monoclonal antibody, for first-line treatment of patients with locally advanced unresectable or metastatic HER2-negative gastric or gastro-esophageal junction adenocarcinoma whose tumors are CLDN18.2-positive.

FDA granted the application priority review and assigned a Prescription Drug User Fee Act date, the FDA action date for their regulatory decision, for Jan. 12, 2024.

Zolbetuximab is sponsored by Astellas Pharma Inc.

The BLA is based on results from the phase III SPOTLIGHT and GLOW clinical trials. The SPOTLIGHT study evaluated zolbetuximab plus mFOLFOX6 (a combination regimen that includes oxaliplatin, leucovorin, and fluorouracil) compared to placebo plus mFOLFOX6. The GLOW study evaluated zolbetuximab plus CAPOX (a combination chemotherapy regimen that includes capcitabine and oxaliplatin) compared to placebo plus CAPOX.

In both SPOTLIGHT and GLOW, approximately 38% of patients screened for the trials had tumors that were CLDN18.2-positive (≥75% of tumor cells with moderate-to-strong membranous CLDN18 staining intensity), as determined by a validated immunohistochemistry assay.

“While rare in the U.S., gastric cancer can be deadly when diagnosed in the late stages,” Moitreyee Chatterjee-Kishore, senior vice president and head of immuno-oncology development at Astellas, said in a statement. “The FDA’s acceptance of the Biologics License Application filing and Priority Review designation for zolbetuximab confirms the urgent therapeutic need and brings us one step closer to delivering on this commitment to patients, families and caregivers.”

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### NCI Trials for July 2023

The National Cancer Institute approved the following clinical research studies last month. For further information, contact the principal investigator listed.

#### Phase I - 10479
A Phase I Dose Escalation-Expansion Trial of Sunitinib Malate Plus Lutetium Lu 177 Dotatate (Lutathera) in Somatostatin Receptor Positive Pancreatic Neuroendocrine Tumors

**Yale University Cancer Center LAO**

Trikalinos, Nikolaos

(857) 202-8301

#### Phase I - 10551
A Phase I/II Study of Anti-CD47 Hu5F9-G4 (Magrolimab) in Combination with Olaparib in Patients with BRCA1/2-Mutant Tumors

**UPMC Hillman Cancer Center LAO**

Mahdi, Haider Salih

(216) 445-7069

#### Phase I - 10572
A Phase 1/2 Trial Evaluating the Combination of Temozolomide and the Ataxia Telangiectasia and Rad3-Related Inhibitor M1774

**Yale University Cancer Center LAO**

Cecchini, Michael

(203) 494-8566

#### Phase II - 10561
Rapid Analysis and Response Evaluation of Combination Anti-Neoplastic Agents in Rare Tumors (RARE CANCER) Trial: RARE 3 Tiragolumab + Atezolizumab

**National Cancer Institute LAO**

Takebe, Naoko

(240) 781-3398

#### Phase II - EAY191-E4
Nilotinib and Paclitaxel in Patients with Prior Taxane-Treated Solid Tumors: A ComboMATCH Treatment Trial

**ECOG-ACRIN Cancer Research Group**

Chen, A P

(301) 402-9122

#### Phase II - S2207
Randomized Phase II Study of the Addition of Targeted Therapeutic Agents to Tafasitamab-Based Therapy in Non-Transplant-Eligible Patients with Relapsed/Refractory Large B-Cell Lymphoma

**SWOG**

Amengual, Jennifer Effie

(212) 305-0591

#### Phase III - EA8211
Phase III Randomized Trial of Stereotactic Ablative Radiotherapy (SABR) for Oligometastatic Advanced Renal Carcinoma (SOAR)

**ECOG-ACRIN Cancer Research Group**

Hannan, Raquibul

(214) 645-7696

#### Phase Other - EAQ221CD
Improving Medication Adherence in Metastatic Breast Cancer Using a Connected Customized Treatment Platform (CONCURxP)

**ECOG-ACRIN Cancer Research Group**

Sadigh, Gelareh

(949) 510-7925