TCL
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Inside information on cancer research and drug development

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# HOW FDA, PFIZER, AND FLATIRON HEALTH DID IT. APPROVAL OF IBRANCE FOR MEN AFFORDS A GLANCE AT USE OF REAL WORLD DATA

Real world data played a role in FDA's recent decision to expand the indications for Pfizer's drug Ibrance (palbociclib) to include men.

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For additional details and to register, please visit the link below:

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REAL WORLD EVIDENCE


# HOW FDA, PFIZER, AND FLATIRON HEALTH DID IT

## APPROVAL OF IBRANCE FOR MEN AFFORDS A GLANCE AT USE OF REAL WORLD DATA

*By Paul Goldberg*

Real world data played a role in FDA's recent decision to expand the indications for Pfizer's drug Ibrance (palbociclib) to include men.

On April 4, Ibrance joined the ranks of cancer drugs that were approved partly based on data extracted from electronic medical records and other data related to actual experience with the drug, as opposed to clinical studies. Approvals relying on such data have been occurring infrequently, and it appears that they haven't been analyzed systematically.

To determine how Pfizer, its collaborator Flatiron Health, and FDA generated and processed RWD and how the agency approached the resulting real world evidence, The Cancer Letter posed a series of questions to FDA, Pfizer and Flatiron.

The answers appear on page 7.

"While no precedent is being set, FDA continues to engage in discussions around generating and using real world evidence to support regulatory decision-making," the agency said in response to questions from The Cancer Letter. "Specifically, FDA's RWE Program will evaluate the potential use of RWE to support changes to labeling about drug product effectiveness, including adding or modifying an indication, such as a change in dose, dose regimen, or route of administration; adding a new population; or adding comparative effectiveness or safety information."

The just-approved sNDA allows Ibrance to be used in combination with an aromatase inhibitor or fulvestrant, and now includes men with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced or metastatic breast cancer.

The drug was approved in 2015 for use in women.

Breast cancer in men is rare. This year 2,670 men would be expected to develop invasive breast cancer, and about 500 will die of metastatic disease.

The approval for use of Ibrance in men is based on data from electronic health records and post-marketing reports of the real world use of Ibrance in male patients sourced from three databases: IQVIA Insurance database, Flatiron Health Breast Cancer database and the Pfizer global safety database.

According to FDA, "the RWE endpoints used were real world tumor response and safety data. Real world tumor response was taken from the electronic health record as part of routine clinical care and information about each response event was retrospectively collected.

> While no precedent is being set, FDA continues to engage in discussions around generating and using real world evidence to support regulatory decision-making.
>
> *– FDA*

"Therefore, this response included several factors, such as physical exam, symptom improvement, and pathology reports, which were used to supplement descriptions of radiology findings in the overall clinicians' assessment of response," the agency said.

A more complete picture of Ibrance will emerge when these data are presented at an upcoming oncology meeting, the company said.

FDA recently created a framework for evaluating the use of real world evidence to support additional indications for already approved drugs as well as to satisfy drug post-marketing study requirements.

The framework lays out the fundamentals of the agency's approach to developing guidances for using real world data in drug regulation. The report, published last December, as required by the 21st Century Cures Act, applies to drugs and biological products. It doesn't apply to medical devices.

In addition to staking out a swath of the burgeoning field of real world evidence, the agency has recruited Amy Abernethy, an expert in generating and applying real world evidence, to the job of principal deputy commissioner, making her the second-highest ranking official at FDA (The Cancer Letter, Jan. 4).

Abernethy is the former chief medical officer, chief scientific officer and senior vice president of oncology at Flatiron Health.

"I think that the major takeaways [from the FDA framework] are consistent with what we were expecting before, which is that there's a move towards trying to understand how to use real world evidence," Abernethy said to The Cancer Letter recently. "And that move is asking, 'How do we make sure that the data quality and the analytic quality is adequate to address the kinds of questions that are going to be brought before the agency?' Really focusing on quality is going to be critical."

Today, RWE is being used for modifying indications, varying doses, adding populations, or including information on safety and effectiveness. To gain in importance, RWE has to be used with the same rigor as clinical trial data, with a clear prospective statistical plan and a prospective definition of success, agency officials say.

Also, databases are far from being able to replace randomized clinical trials, because RCTs have the capacity to measure impact of factors that aren't known to researchers and therefore cannot be incorporated into RWE models.

Pfizer's Ibrance is now approved for adult patients with HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men; or with fulvestrant in patients with disease progression following endocrine therapy.

With the latest approval, Ibrance becomes the first and only CDK 4/6 inhibitor indicated in combination with an aromatase inhibitor for the first-line treatment of men with HR+, HER2- metastatic breast cancer in the U.S.

The prescribing information for Ibrance can be found here.

*Matthew Bin Han Ong contributed to this story.*

REAL WORLD EVIDENCE


# How real world evidence was used to support approval of Ibrance for male breast cancer

We posed the same 10 questions to FDA, Pfizer and Flatiron Health.

Here is what came back:

**The Cancer Letter: Was this the first approval based at least in part on real world evidence in oncology?**

**FDA:** Ibrance (palbociclib) was initially approved in 2015. It is a kinase inhibitor, now approved in combination with an aromatase inhibitor as the first hormonal-based therapy in women who have gone through menopause and in men, or with fulvestrant in patients whose disease progressed following hormonal therapy.

Pfizer provided the results of an analysis of real world data (RWD) from electronic health records (EHRs) as additional supportive data to characterize the use of Ibrance in combination with endocrine therapy (aromatase inhibitor or fulvestrant) in male patients with breast cancer based on observed tumor responses in this rare subset of patients with breast cancer.

Leveraging RWD to improve regulatory decisions is a key strategic priority for the FDA. This data may be derived from a variety of sources, such as electronic health records, medical claims, product and disease registries, laboratory test results and even cutting-edge technology paired with mobile devices.

These types of data are being used to develop real world evidence (RWE) that can better inform regulatory decisions.

Because they include data covering the experience of physicians and patients with the actual use of new treatments in practice, and not just in research studies, the collective evaluation of these data sources has the potential to inform clinical decision-making by patients and providers, develop new hypotheses for further testing of new products to drive continued innovation and inform us about the performance of medical products.

FDA has previously accepted RWD to support drug product approvals, primarily in the setting of oncology and rare diseases.

RWD has been used to determine prognosis or natural history of disease in order to help inform regulatory decision-making, for example, data on historical response rates drawn from expanded access, practice settings, or chart reviews.

**Chris Boshoff, chief development officer, oncology, Pfizer Global Product Development:** Defer to FDA.

**Ken Carson, senior medical director, Flatiron Health:** Defer to FDA.

**TCL: What were the RWE endpoints being used here?**

**FDA:** The RWE endpoints used were real world tumor response and safety data. Real world tumor response was taken from the electronic health record as part of routine clinical care and information about each response event was retrospectively collected.

Therefore, this response included several factors, such as physical exam, symptom improvement, and pathology reports, which were used to supplement descriptions of radiology findings in the overall clinicians' assessment of response.

Additional data on use and durations of prescriptions were also provided.

**Pfizer:** The expanded indication in breast cancer is based on limited data from post-marketing reports and electronic health records sourced from three databases: IQVIA Insurance database, Flatiron Health Breast Cancer database and the Pfizer global safety database.

Based on these limited data, the safety profile for men treated with IBRANCE is consistent with the safety profile in women treated with IBRANCE.

A detailed analysis of the use of IBRANCE in men with HR+, HER2- advanced or metastatic breast cancer will be presented at an upcoming medical meeting.

**Flatiron:** For this dataset, Pfizer engaged Flatiron to explore baseline characteristics, treatment patterns and clinical outcomes from patient-level, de-identified data for a group of male patients with metastatic breast cancer.

As with any project in which a partner is considering the inclusion of RWE as part of a regulatory submission, we consider it critical to ensure the data is "fit-for-purpose," that is, ensuring that the dataset is fit for the intended use and can provide adequate scientific evidence.

**TCL: Why was this application the right setting to use RWE?**

**FDA:** Breast cancer is rare in males, with only 2,670 cases of male breast cancer estimated in 2019—less than 1% of all cases of breast cancer.

Due to the rarity of male breast cancer, there is limited evidence available to guide treatment decisions and it is not feasible to conduct prospective clinical studies.

FDA has previously extrapolated efficacy and safety by granting indications in breast cancer to male patients, even if no male breast cancer patients were enrolled in the supporting trial.

However, in certain cases when there is the potential of differential efficacy or safety results between men and women with breast cancer, such as when a drug is combined with endocrine therapy and results in or relies upon manipulation of the hormonal axis, further evidence may be necessary to support a labeling indication for male patients.

This need for additional evidence, combined with the rarity of male breast cancer, made this the right setting to use RWD.

**Pfizer:** Real world data are playing an increasingly important role in expanding the use of already-approved innovative medicines.

The 21st Century Cures Act, enacted in 2016, was created to help accelerate medical product development, allowing new innovations and advances to become available to patients who need them faster and more efficiently.

This law places additional focus on the use of real world data to support regulatory decision-making.

Further, the rarity of male breast cancer can make it difficult to recruit a significant number of patients for a formal clinical trial.

The expanded indication in breast cancer is based on limited data from post-marketing reports and electronic health records, and we're pleased to have played a role in this innovative approach that now provides a much-needed option for men living with HR+, HER2- MBC.

**Flatiron:** Given the potentially challenging and time-consuming process (source) of accruing patients as part of a prospective clinical trial in rare cohorts such as males with metastatic breast cancer, using RWE to pursue an indication in this population held the potential to provide an avenue to support regulatory approval.

However, as with any decision impacting patient care and treatment, the "fit for purpose" of RWE must always be considered.

**TCL: To what extent was RWE used—as primary evidence or as confirmatory evidence?**

**FDA:** Certain treatments for metastatic breast cancer are gender-neutral in their indication, but some therapies have been approved only for women, although they are often prescribed for male patients.

The safety and efficacy of Ibrance had been previously demonstrated in women and therefore was only supported by RWD in order to extend the indication to men.

The initial studies of Ibrance in breast cancer did not enroll male patients and thus this supportive RWD information was helpful to further assess the ability to extend the indication to this rare subgroup of patients.

**Pfizer:** The expanded indication in breast cancer is based on limited data from post-marketing reports and electronic health records sourced from three databases: IQVIA Insurance database, Flatiron Health Breast Cancer database and the Pfizer global safety database.

Based on these limited data, the safety profile for men treated with Ibrance is consistent with the safety profile in women treated with Ibrance.

Defer to FDA for additional information.

**Flatiron:** The dataset provided by Flatiron, along with other data sources, was used as primary evidence within Pfizer's supplemental NDA submission.

**TCL: Which conventional endpoints were the RWE endpoints being tied to? What gives you comfort that these are equivalent metrics?**

**FDA:** Real world tumor response is related to objective response rate, but these are not considered equivalent metrics. RWD provides insight into how providers administer the drug, and while there are limitations to real world tumor response, this endpoint provides an estimate of drug response and benefit.

**Pfizer:** Based on limited data from post-marketing reports and electronic health records, the safety profile for men treated with Ibrance is consistent with the safety profile in women treated with Ibrance.

The efficacy and safety of Ibrance in women with HR+, HER2- metastatic breast cancer is supported by robust clinical trial data from three randomized pivotal trials across the PALOMA program that consistently demonstrated a meaningful PFS benefit.

Today in the U.S., Ibrance is the most prescribed FDA-approved oral combination treatment for HR+, HER2- MBC. Ibrance currently is approved in more than 90 countries and has been prescribed to more than 200,000 patients globally.

A detailed analysis of the use of Ibrance in men with HR+, HER2- advanced or metastatic breast cancer will be presented at an upcoming medical meeting

**Flatiron:** There are important distinctions between assessing endpoints in the real world versus a clinical trial setting (which is what we take to be implied by "conventional").

Endpoints collected through randomized clinical oncology trials such a tumor response, progression, and treatment-related toxicity are collected intentionally, with pre-specified methods at fixed time intervals.

Endpoints in real world data are collected within the patients' medical records and later incorporated into a study dataset.

For this project, we did not compare endpoints to a clinical trial or "conventional" endpoints. However, we have previously performed exercises which have demonstrated clinically appropriate correlations between endpoints such as real world progression and real world overall survival and their conventional counterpoints.

**TCL: What was the FDA's role in deciding which RWE endpoints were to be used?**

**FDA:** Multiple conversations between the FDA and the company allowed for determination of appropriate endpoints and the amount of data needed prior to the submission.

As with all of our reviews, during this review cycle, information was requested of the company and exchanged back to FDA clarifying individual data elements and narratives.

**Pfizer:** Defer to FDA.

**Flatiron:** Defer to FDA.

**TCL: How were the RWE data sources selected? How were these databases harmonized in terms of data collection standards?**

**FDA:** While there are multiple potential RWE data sources, through discussions with the company, appropriate sources, endpoints, and the amount of information that would be required for a full review were selected.

FDA is currently in the process of developing set data standards for regulatory use and will continue to expand its work in this area.

**Pfizer:** A detailed analysis of the use of Ibrance in men with HR+, HER2- ad-

vanced or metastatic breast cancer will be presented at an upcoming medical meeting.

**Flatiron:** Defer to Pfizer.

**TCL: What's the take-away message here? What can oncology learn about what it takes to generate regulatory-grade RWE?**

**FDA:** We were able to use the extensive substantial evidence of safety and effectiveness that Ibrance had previously demonstrated in women and supporting RWD in order to extend the indication to men.

The FDA recognizes the importance of RWD/RWE and is committed to realizing the full potential of these tools in advancing the development of treatments for patients.

In December 2018, the FDA published a Framework for the RWE program to apply across our programs. We are committed to leveraging information gathered from the medical community and patients to help inform our regulatory decisions regarding drug and biologic development efforts.

**Pfizer:** We appreciate that our partnership with the FDA has allowed us to take a significant step forward in the use of real world data to bring medicines to patients who are most in need.

Real world data are playing an increasingly important role in expanding the use of already approved, innovative medicines.

The 21st Century Cures Act, enacted in 2016, was created to help accelerate medical product development, allowing new innovations and advances to become available to patients who need them faster and more efficiently. This law places additional focus on the use of real world data to support regulatory decision making.

A detailed analysis of the use of Ibrance in men with HR+, HER2- advanced or metastatic breast cancer will be presented at an upcoming medical meeting.

**Flatiron:** RWD can serve as a strong evidence source, enabling us to learn from patients who are being treated in the real world and reinvest those learnings back into research to help future patients.

The FDA's acceptance of RWE as part of this submission is consistent with implementing the draft framework that the agency outlined in December 2018, and is another critical datapoint in the FDA's evolving position regarding RWE.

Flatiron continues to be optimistic about the possibility of RWE in the appropriate circumstances to support regulatory decision-making, and appreciates the FDA's leadership and collaboration in these efforts.

**TCL: Is there a precedent being set here, and if so what is it?**

**FDA:** While no precedent is being set, FDA continues to engage in discussions around generating and using RWE to support regulatory decision-making.

Specifically, FDA's RWE Program will evaluate the potential use of RWE to support changes to labeling about drug product effectiveness, including adding or modifying an indication, such as a change in dose, dose regimen, or route of administration; adding a new population; or adding comparative effectiveness or safety information.

**Pfizer:** Defer to FDA.

**Flatiron:** Defer to FDA.

**TCL: Is there anything you'd like to add?**

**FDA:** The RWE Program will involve the establishment of demonstration projects, engagement with stakeholders, the use of internal processes that bring senior leadership input into the evaluation of RWE and promote shared learning and consistency in applying the framework, and the development of guidance documents to assist sponsors interested in using RWE to support their work.

As part of its RWE Program, FDA will also evaluate the potential role of observational studies in contributing to evidence of drug product effectiveness. Efforts to replicate the results of randomized controlled trials using more rigorously designed observational studies may provide insight into the opportunities and limitations of using these designs in regulatory decisions.

FDA is committed to advancing the use of RWE and looks forward to working with companies to further advance the field. As the reliability RWE data improves and the data collection science evolves, we hope to be able to use RWE as primary evidence supporting an approval.

**Pfizer:** This approval represents a significant step forward in the use of real world data, particularly for underserved populations.

With this approval, Ibrance is the first and only CDK 4/6 inhibitor in the U.S. indicated in combination with an aromatase inhibitor for the first-line treatment of men living with HR+, HER2- metastatic breast cancer, further reinforcing Pfizer's deep commitment to putting patients first and meeting unmet treatment needs with our innovative medicines.

# NCI advisors approve eight concepts, including three Cancer Moonshot concepts

*By Claire Dietz*

The NCI Board of Scientific Advisors approved eight new Requests for Applications, Requests for Proposals, and PAR—a program announcement reviewed in the institute—concepts at a meeting March 25, including three new Cancer Moonshot concepts.

One Cancer Moonshot concept, "Technologies Development for Use in Next Generation Cancer Models," was deferred at the last BSA meeting in December (The Cancer Letter, Jan. 11).

The following concepts were approved:

## Cancer Intervention and Surveillance Modeling Network (re-issue RFA/Coop. Agr.)

This RFA is focused on the Cancer Intervention and Surveillance Modeling Network, CISNET, formed in 2000, which is an NCI-sponsored collaborative consortium of simulation modelers in breast, prostate, colorectal, lung, esophagus, and cervical cancers.

Using simulation modeling, CISNET extends evidence provided by trials and both epidemiologic and surveillance data to guide public health research and priorities. It also helps address the gap between innovation in cancer research and the "ability to efficiently harness it to improve population health."

The RFA was submitted by project scientists from the Division of Cancer Prevention and the Division of Cancer Control and Population Sciences.

According to the RFA, in many instances, individual modeling efforts yields different results which are difficult to reconcile. CISNET created a new approach called systematic comparative modeling. This modeling uses central questions to be addressed by groups collaboratively with a common set of inputs and outputs. It aims for reproducibility across models to add credibility to the results, and differences point out areas for further study in a systematic way.

The RFA proposed components for the next round of CISNET, which included an open competition, including the continuation of current cancer sites with up to six multiple-PI U01's. A U01 is a cooperative agreement aimed to "support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing his or her specific interest and competencies."

CISNET proposed the continuation of several cross-program activities including continued cross-cancer site collaborations, continued programmers interest group, and the new program: Junior Investigators Career Enhancement program, known as JUICE.

According to the RFA, CISNET can help answer questions that are becoming ubiquitous in oncology. These questions were broken up by type of cancer:

- Cervical: Should screening recommendations change as vaccinated populations reach screening age?
- Colorectal: What mix of screen modalities for colorectal cancer might

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work best in underserved populated in the U.S. and in middle- and lower-income countries?

- Breast: Can the interface between randomized trials of active surveillance for DCIS (ductal carcinoma in situ) of the breast and modeling help us better understand and manage this condition?
- Esophageal: Can low cost, minimally invasive mass screening serve as a cost-effective triage for upper endoscopy to detect Barrett's esophagus?
- Prostate: Are the strategies for PSA screen that more effectively "threading the needle" of maximizing mortality reduction while minimizing overdiagnosis? What are the most effective strategies for initiating and terminating active surveillance that can minimize the harms of overdiagnosis?
- Lung: What strategies for the management of suspicious nodules (Lung-Rads, volumetrics) are most effective for minimizing false positives, while maximizing sensitivity? Could strategies be individualized to take into account personal preferences?

The RFA's nine priority areas to focus their modeling efforts are:

- Precision screening and new screening technologies
- Prevision treatment
- Overdiagnosis and active surveillance
- Decision aids (individual and policy)
- Understanding screening in real-world settings and determining the best routes to optimize the processes
- State, local, and international cancer control planning
- Suggesting optimal routes to reduce health disparities
- Methods development
- Cancer site-specific opportunities

The ongoing priorities for the RFA set by Organ Sites Specific Steering Committees:

- Specific aims as specified in grant application and selected from the priority areas
- New topics of timely relevance
- Outside inquiries from other NCI staff, NCI sponsored consortia, guideline setting organizations, and other outside researchers and organizations

In keeping pace with precision treatment, CISNET will focus on evolving big data resources drawn from electronic claims, labs, and health records, and their potential linkage to population-based registry data. This would generate detailed information on first-line and salvage therapies as well as dose, recurrence, and the genomic characterization of disease.

The Junior Investigators Career Enhancement Program is aimed to address the fact that modeling-oriented data scientists are in high demand and short supply.

The program is designed to help junior investigators to get the most out of their CISNET experiences and primarily targets pre-docs, post-docs, and junior faculty across CISNET. In the last round of CISNET, there were junior investigators initiative sponsored webinars, lunch sessions at meetings, and networking opportunities—but this was still a largely underfunded mandate, according to the RFA.

The budget places strict constraints on direct costs per year for each component. This included

- $180k per modeling group (with three to six groups)
- $110k for coordinating center
- $100k for rapid response funds
- $40k for the JUICE program.

The total cost per year for six awards (with an average of four modeling groups per cancer site) was about $1.66 million for each award, or $10 million for all six awards. From fiscal year 2020 to fiscal year 2024, the total budget would be $50 million.

## AIDS Malignancy Consortium (re-issue RFA/Coop. Agr./Ltd. Competition)

Approximately 36.7 million people live with HIV worldwide, with approximately 1.8 million new infections per year. Cancer is a prominent manifestation of HIV/AIDS and is a leading cause of morbidity and mortality in HIV-infected people.

The AIDS Malignancy Consortium's mission is to:

- Develop and evaluate clinical interventions for the treatment and prevention of malignancies in people with HIV
- Conduct phase I, II, and III clinical trials of HIV-related malignancies
- Investigate the biology of these malignancies in the context of clinical trials
- Contribute specimens and clinical data to the AIDS and Cancer Specimen Resource.

In this grant cycle, the past 36 months, the consortium has developed 15 protocols, with 14 protocols having completed enrollment. Almost 2,900 patients have been accrued, with 2,350 in the ANCHOR study, and 537 non-ANCHOR participants. Fourteen protocols are actively accruing patients and approximately 63% of accrued U.S. participants are African American or Hispanic in origin. In the past 3 years, approximately 39 papers have been published in peer-reviewed journals.

The ANCHOR study, Anal Cancer HSIL Outcomes Research study, is a randomized controlled trial to establish whether treatment of anal high grade squamous intraepithelial lesions is an effective strategy in preventing anal cancer and will evaluate whether screening for HSIL is warranted.

Over 5,000 patients with HSIL will be randomized to two arms, treatment or active monitoring. To date, more than 7,000 have been screened and 2,804 have been randomized. The study will establish a bank of blood, anal swabs, and tissue specimens to study the molecular pathogenesis of progression from HSIL to cancer.

The consortium's accomplishments this grant cycle include:

- Evaluating immunotherapy approaches to solid tumors in HIV patients, using ipilimumab and nivolumab in advance solid tumors and brentuximab vedotin, or nivolumab for Hodgkin lymphoma
- Developing and the assessment of new approaches for the front-line treatment of AIDS lymphoma (ibrutinib and R-DA-EPOCH and vorinostat and R-DA-EPOCH)
- Investigating treatments with novel mechanisms of action for Kaposi sarcoma (bortezomib, lenalidomide, sEphB4-HAS)
- Conducting Kaposi sarcoma international trials that defined standard of care in limited resource settings
- Providing evidence for efficacy of the HPV vaccine in preventing HSIL among HIV-infected individuals naïve to the vaccine type
- Assessing a therapeutic vaccine directed to E6/E7 HPV types 16/18 genes using electroporation
- Establishing a network of clinicians trained in high resolution anoscopy and treating anal HSIL. These treatments and platform are being used for the conduct of the ANCHOR study
- Completing a feasibility study in Africa of the safety, toxicity, and compliance of concomitant chemotherapy and radiotherapy for HIV-associated locally-advanced cervical cancer
- Examining pharmacokinetic interactions of antiretroviral agents and novel anti-cancer agents (sunitinib, cabozentinib) in HIV subjects with solid tumors

The consortium's "Practice-Changing Accomplishment[s]" include:

- Establishing the standards for chemotherapy in aggressive CD20+ AIDS-related lymphomas, including the use of combination anti-retroviral therapy with rituximab-CHOP
- Helping establish treatment standard for drug-resistant severe Kaposi sarcoma (paclitaxel) and assessing the relative merits of the two most efficacious drugs (paclitaxel vs liposomal doxorubicin)
- Establishing infrared coagulation as the leading method of treatment of anal high grade squamous interepithelial lesions
- Establishing the superiority of paclitaxel over etoposide or bleomycin/vincristine (the previous standard of care) for treating Kaposi sarcoma in Africa
- Demonstrating that HIV-associated aggressive lymphoma patients who meet standard eligibility criteria for autologous or allogenic stem cell transplant responds well to transplantation (This is now the standard of care)
- Developing and initiating the ANCHOR trial, they said it will likely define standard for anal cancer screening. The study is more than half accrued

The consortium's current scientific needs are:

- Cancer continues to be among the leading causes of death among HIV-infected patients in the U.S., and in some studies, it is the leading cause
- The standards of care for progressive Kaposi sarcoma and NHL have not been optimized
- Non-AIDS-defining cancers (especially lung, liver, head and neck, and anal) are increasing in areas where cART is widely available
- The impact of AIDS and cART on anti-cancer chemotherapy, on toxicity profiles, and on response to treatment are not sufficiently studied
- Need to optimize treatment in resource-limited countries

The total proposed budget for the RFA 5 years is $113,730,523.

## Cancer Trials Support Unit contract renewal proposal (re-issue RFP)

The Cancer Trials Support Unit is a service of the NCI that supports clinical trial management and conduct. It "provides services to NCI-sponsored programs

such as the National Clinical Trials Network, the Experimental Therapeutics Clinical Trials Network, and the NCI Community Oncology Research Program," as well as other programs.

CTSU was established in 1999 to "streamline and harmonize support services for Phase III Cooperative Group cancer clinical trials funded by the NCI." The scope of the unit has expanded to include support of multiple NCI-funded networks and clinical trials in the realm of cancer treatment, prevention and control, advanced imaging, and correlative science studies.

Their objectives are:

- Providing centralized operational support activities for NCI Clinical Trials conducted by the NCTN, ETCTN, NCORP, and other multi-center organizations
- Facilitating investigator/research staff participation in NCI multi-center programs/clinical trials
- Increasing investigator and patient awareness and enrollment
- Providing standardized, integrated, and comprehensive support services
- Identifying best practices and streamline or eliminate redundant processes
- Improving operational efficiency, enhance productivity and deliver products offering measurable business value

CTSU helps provide 24/7 operational support for the entire lifecycle of a clinical trial. It also supports an NCI Grant portfolio with a combined FY2019 funding level of about $343 million per year. CTSU's budget only takes up about $23 million a year, which is approximately 5-6% of the entire grant portfolio budget.

The program helps streamline the pre-enrollment process, subject enrollment—a process which has multiple checks to ensure compliance—and study conduct and monitoring.

The unit's accomplishments include:

- Supporting transition to NCTN/NCORP/ETCTN
- CDMS Integration across networks
- Supporting precision medicine trials (MATCH, Exceptional Responders, LUNG-MAP)
- Implementing biospecimen navigator
- Safety database integration
- Implementing data standardization across networks
- Supporting increased regulatory compliance
  - Registration and credential repository
  - Delegation of tasks log
  - CDISC compliance
- Site support for Electronic Medical Record/National Coverage Analysis

The program's future goals include optimizing their current services and integrations in order to increase efficiency, including by:

- Maintaining and enhancing operational, administrative, regulatory support of current Grant portfolios and new Grantees as identified
- Maintaining and enhancing integration activities/standardization
- Leveraging multiple contractors as opposed to a single contractor
  - They plan to divide contract service areas into smaller units, which gives them flexibility to address new needs/regulations/requirements, and emerging technologies.
- Increasing Contract awardee pool
  - Current contract includes: 2 awardees, Future contract: 4-8 awardees

The budget request for the contract reissue is for a 10-year contract period, with a requested budget of $23 million per year, which represents a small decrease over the average expenditure of current contract. It also includes an allowance for cost-of-living adjustments.

## Small Business Innovation Research Proposed FY2020 Contract Topics (new RFP)

The Small Business Innovation Research and Small Business Technology Transfer programs are housed in the Office of the Director at NCI.

Under the SBIR program, the contract mechanism is primarily used to fund awards in targeted areas of research and development that are "ripe for development by the small business community," said Andrew Kurtz, program director and team leader at NCI's SBIR and STTR programs.

"These tend to be areas that the NCI has identified as being priorities for the institute. In a lot of cases they are intended to fill in technology gaps, areas that the private sector hasn't adequately addressed on its own or things that are intended to support some of the broader research goals of the institute," Kurtz said to The Cancer Letter.

The NCI's SBIR and STTR programs take a small portion of NCI's overall extramural research and development funding. The SBIR program is required to spend 3.2% of NCI's extramural research and development budget on projects at U.S. small businesses.

"A majority of our SBIR funding goes toward funding investigator-initiated grant awards, where the companies bring their best ideas to the NCI," Kurtz said.

The portion of the SBIR budget used to fund contracts in targeted areas may fall anywhere from 10-20%, though it varies by year.

One case Kurtz gave as an example included MagArray Inc., whose goal was to develop sensors with improved sensitivity and specificity of genomic and proteomic signatures for early detection and post-treatment monitoring.

A Stanford spin-out, MarArray worked with ultra-sensitive multiplex immunoassay systems, which ultimately resulted in REVEAL Blood Test for Lung Nodule Characterization, which launched in 2018, after receiving the Phase I contract in 2007.

## Clinical characterization of cancer therapy-induced adverse sequelae and mechanism-based interventional strategies (new PAR)

Cancer treatments can result in acute, chronic, or progressive toxicities with adverse effects persisting after completion of therapy or developing as late effects. Cancer survivorship and adverse effects will significantly increase in the next couple of decades, but little is known about the rates of adverse events related to new therapies.

Currently, the development of biomarkers and the mitigation and prevention strategies are limited by:

- Lack of mechanistic understanding of adverse events
- Lack of accurate reporting and archiving of adverse event data
- Difficulties in objectively measuring treatment-related toxic effects
- Insufficient characterization of the clinical phenotypes
- Insufficient studies validating pre-clinical biomarkers in the clinical setting

The purpose of the program announcement with special review was to:

- Support preclinical and clinical research projects which seek to:
  - Clinically characterize adverse sequelae
  - Translate the mechanistic understanding into therapeutic approaches to prevent or minimize the development of long-term sequelae
  - Identify mechanisms of new therapy-induced adverse sequelae
- Applications should prospectively identify the specific adverse effects and/or cluster of effects under evaluation
- Collaborations between clinical and non-clinical investigators are encouraged to couple the Mechanistic knowledge with the clinical phenotype
- Emphasizing should be on translating mechanistic knowledge into approaches or interventions to prevent or mitigate adverse sequelae

The PAR would:

- Stimulate clinical and translational research related to adverse-effects with strong mechanistic underpinnings that:
  - Go beyond single adverse-effects to look at clusters of effects
  - Address newly identified adverse-effects related to treatment
  - Characterize clinical phenotypes of adverse-effects
  - Evaluate and/or validate new biomarkers
  - Evaluate the trajectory of chronic or progressive adverse-effects and their relationship with cancer treatments and other comorbid conditions
  - Develop intervention strategies
- Applications that evaluate clinical characteristics and mechanisms of adverse sequelae tend to be poorly reviewed in NIH standing study sections (which lack expertise in treatment relative adverse effects)

The PAR would also:

- Leverage NCI investment to:
  - Clinically characterize adverse sequelae
  - Translate the mechanistic understanding into therapeutic approaches to prevent or minimize the development of long-term sequelae
  - Identify mechanisms of new therapy-induced adverse sequelae

- Specific review panels are critical

***Three Cancer Moonshot concepts were approved:***

## Activities to Promote Human Immune-Representing Oncology Models (RFA)

The RFA aims to support "new model development research projects proposing to recapitulate innate and adaptive components of the human immune system without the use of human fetal tissue, in a manner that addresses the needs of immuno-oncology research." These models must demonstrate recapitulation of human immune function.

The RFA proposes research projects that focus on "recapitulation of the human immune system in their proposed cancer model using human cells or tissues to regenerate and recapitulate the human immune system in in-vivo or in-vitro immuno-oncology models in a manner that matches or exceeds representation of the human immune system achieved with murine models developed using human fetal tissue.".

The award would have a single receipt date, anticipating support for two to three R33 projects with a maximum budget of $250,000 direct costs per year for up to 4 years (which is adequate to support multi-PI teams). It accounts for up to $4 million in total cost. The anticipated schedule:

- April 2019: Issue "Notice of Intent to Publish"
- June/July 2019: Publish RFA
- Nov/Dec 2019: Application Due Date
- June 2020: Award Date/ Project Start Date

The outcome measures include both development and dissemination measures. The development measures include exhibiting capabilities that support replacement of models developed using human fetal tissue, the number of projects that meet their proposed performance measures, publications demonstrating progress towards proposed aims, and evidence of subsequent investment to pursue dissemination.

The dissemination measures include: the number of new collaborations explored by supported model developers and investigators associated with immuno-oncology research and the number of models that are adopted by immuno-oncology research groups—especially those replacing models developed using human fetal tissue.

## Next Gen Technology for Next Gen Cancer Models (RFA)

This Cancer Moonshot concept was a reissue from a previous BSA meeting in December 2018.

The Human Cancer Models Initiative is an international consortium with approximately 1000 "next generation human cancer models" with clinical and molecular data. This consortium includes NCI's Moonshot initiative, Wellcome Sanger Institute, and Hubrecht Organoid Technology.

Some of the technologies for model development include organoids and conditionally reprogrammed cells.

The challenge of the concept rationale was: functional genomic technologies are not optimized for efficient use in next-gen cancer models. Successful completion of this concept will fill gaps, as well as answering several questions:

- What is the impact of cellular polarity in 3D structures on the results from perturbagen screens?
  - Does topology (e.g. 3D organoids) change the effect of gene(s) essentiality in cancer?
- How to adapt pertubagens that were developed for classical cancer cell lines to function in other cancer models?
- What transduction technologies should be optimized for 3D and 2D NGCM?
  - Can diffusion work efficiently for cells that are within (internal) an organoid?

The concept's goals are:

- The NGCMs represent a powerful tool for precision oncology
  - Clinical data, including response to treatment of donor patient
  - Genomic characterization upfront
  - This FOA aims to accelerate functional genomics using the HCMI models in screens using:
  - Cas9/gRNA (CRISPR)
  - RNAi
  - Open reading frame cDNA
  - Small molecule

The concept will address the technical challenges of "using NGCM in functional genomics experiments and applications" and will do so by developing of robust protocols and conditions when using molecular perturbagens (Cas9/gRNAs, small molecules, cDNAs) with NGCMs and rapid sharing of all data and reagents.

The methods, data and reagents generated under the FOA will allow research-

ers to get insight into essential pathways in cancer. The preclinical knowledge base will support precision oncology by identifying new drug targets and mechanisms of therapeutic resistance.

Advantages of the consortium include:

- The grant awardees will use NGCMs developed through NCI's investment in the HCMI program
- Research in the cooperative U01 setting will:
  - Reduce excessive redundancy, thereby ensure cost efficiency
  - Promote sharing of reagents and communication
  - Standardize methods
  - Provide standardized reagents
  - Make all data publicly available
- The contract mechanism requires deliverables and oversight
- A single steering committee allows real-time sharing of results between the U01 Centers and contractor

The funding for this concept would include FY2020-2022. The U01 Technology Centers, which would be about three in total, would have an estimated $3.3 million per year cost. The Standardized Reagent Developer contract, which involves CRISPR reagents development and distribution, would cost roughly $700,000 per year. The total cost of the concept would be $4 million per year, or $12 million over the three years.

## Therapeutic Target Identification to Overcome Drug Resistance (RFA)

The Drug Resistance & Sensitivity Network was funded under RFA-CA-17-009, which is composed of U54 centers, and was launched in FY18. A new FY20 initiative, "Mechanisms of Cancer Drug Resistance Competing Revisions" provides rationale for a complementary initiative, leverages the wider range of expertise in the NCI portfolio, encourages collaborative projects, as well as incentivizes and accelerates ideas not well represented in the DRSN.

DRSN's overarching focus is to address the Blue Ribbon Panel recommendation on establishment of multidisciplinary research teams to elucidate the complex mechanistic underpinnings of drug resistance and to inform drug development efforts and future clinical trials:

- Drug Resistance & Sensitivity Network composed of 5 x U54s, launched in FY18
- These U54s are primarily disease-specific
- Preference given to studies involving NCI CTEP IND agents
- NCI-IND agents (n= >60) include a wide variety of small molecule and antibody inhibitors that impact classic oncogenic signaling, epigenetic regulators & checkpoint targets (e.g., RTK, MAPK, AR, EZH2, PDL1)

DSRN's goal for the Competing Revision initiative is to accelerate evaluation of: new and/or under-explored mechanisms of drug resistance, new approaches with classical targets, and promote collaborative efforts that complement on-going DRSN studies. It also aims to:

- Leverage active broad-based NCI research programs that have the capability to incorporate new directions and accompanying know-how/expertise;
- Competing Revision opportunities will incentivize new collaboration, enable testing of new concepts in drug resistance, and accelerate on-going activities represented in the DRSN;
- Identify and characterize new leads for DRSN and other NCI activities;
- Potential to inform and accelerate the development of therapeutic targets in a synergistic manner;
- Opportunity to expand and diversify the current DRSN

The funding structure of DSRN:

- Variety of mechanisms are eligible (R01, U01, P01, U54, P50);
- Programmatic expectations for responsiveness:
  - involves multi-disciplinary scientific collaborations;
  - brings together complementary expertise;
  - promotes infusion of a new cadre of investigators into DRSN efforts; and
  - accelerates ideas that align and integrate with the overarching objectives of the BRP recommendation;
- Anticipate funding 5 to 10 new competing supplements (4 receipt dates over 2 years);
- Budgetary requests may not exceed $250,000 D.C./year for the life of the project;
- Applicants must have a minimum of 3 years left of funding on the parent grant (at the time of application);

The total cost of the Moonshot concept would be $4.2 million per year, and $12.6 million in total over the next three fiscal years.

## LETTERS TO THE EDITOR

To the editor:

My name is Niko Fotopoulos, and I am currently a sophomore studying molecular biology at Princeton University.

I read your article on robotic assisted mastectomy. I also read the follow-up letter by Dr. Chagares and Mr. Goldberg's response with questions attached. While I may be of some help, I am precluded from many specifics, as I am the clinical researcher on the IRB/Clinical Trial that was submitted and unanimously approved at Monmouth Medical Center. Also, as a student of science, I stand behind my work product.

I met and observed Dr. Toesca when I traveled with Dr. Chagares to Milan, Italy. I assisted Dr. Chagares in New Jersey when we used Dr. Toesca's clinical trial as the blueprint to create the one submitted to Monmouth Medical Center.

I prepared a multitude of correspondence for the IRB and clinical trial process and extensively prepared for the IRB committee presentation. I took part in the extensive review process as the IRB department had edits, changes, requests and clarifications along the extremely detailed process over the course of multiple months.

Additionally, for the first procedure, I coordinated directly with Dr. Toesca for his proctoring of the surgery and any requests he made to assure the safety of the procedure.

My apologies for not being able to share specifics of the clinical trial. As far as FDA/Regulatory/IDE questions, I would not be able to assist with those answers, as those decisions were made by the hospital IRB office.

The clinical trial was extensively vetted by the IRB committee and received unanimous approval.

Best,

Nicholas Fotopoulos
Princeton Class of 2021
AB Molecular Biology with Certificate in Entrepreneurship

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To the editor:

My name is Brian Thomson, and I am a patient of Dr. Chagares's. I read your article on robotic mastectomy, and I want to clarify that the article is not accurate. On Sept. 28, 2018, Dr. Chagares performed my robotic assisted bilateral mastectomy at Monmouth Medical Center.

Prior to my surgery, I had consultations with Dr. Chagares and a full work up. Dr. Chagares gave me several surgical options to remove the masses in my breasts.

Dr. Chagares clearly explained that the robotic approach was in an IRB/Clinical Trial. He also explained that Dr. Toesca from Milan, Italy, trained him, and confirmed that I would be the first male robotic mastectomy performed worldwide.

We discussed the risks, benefits and complications of the surgery. We discussed the protocol of the clinical trial and what would be required of me after surgery.

Dr. Chagares explained that I would need to continue to see him twice a year for physical examinations and to complete a questionnaire at each visit so he can collect the information for his long-term trial.

Dr. Chagares and his staff spent an unbelievable amount of time answering all of my questions and explaining the surgery to me.

I felt very comfortable making the decision that the robotic assisted mastectomy was the approach for me. I signed the Monmouth Medical Center consent for surgery along with the Monmouth Medical Center documents consenting to participate in an IRB/Clinical Trial.

My experience with Dr. Chagares was absolutely outstanding.

I hope this helps clarify the inaccuracy of your article.

Thank you,

Brian Thomson

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***The editor responds:*** *The Cancer Letter is grateful to Mr. Fotopoulos and Mr. Thomson for writing to us.*

*Because of incorrect information provided to us, The Cancer Letter reported erroneously that Dr. Stephen Chagares had performed two robotic mastectomies without a protocol (The Cancer Letter, April 5).*

*This was a minor part of a story about the controversial procedure that is considered investigational.*

*While the rest of our reporting stands, we have annotated the original story to reflect the error, posed a series of questions to Monmouth Medical Center and Dr. Chagares, and published a correction.*

*Reporting on this story is ongoing.*

AAADV

Accelerating Anticancer Agent Development and Validation

# 16th Annual Accelerating Anticancer Agent Development and Validation (AAADV) Workshop

May 8-10, 2019,
North Bethesda, Maryland

## ABOUT THE AAADV WORKSHOP

Leaders in clinical and translational cancer research from academia, industry, government and nonprofit advocacy sectors convene each spring in North Bethesda, Maryland, for the AAADV Workshop, a unique forum designed to speed cancer treatments to patients.

This three-day, on-site interactive workshop offers a mix of small group lectures, moderated discussions, plenary lectures and facilitated case studies of successful drug applications.

**Travel and Housing Scholarships Available for Academicians and Patient Advocates**

Participants gain valuable insights on negotiating the spectrum of successful drug development and hone their strategic planning skills with a focus on target validation and pathway identification.

AAADV is the only workshop held in collaboration with the U.S. Food and Drug Administration designed specifically to help participants understand and negotiate the drug development approval process so effective cancer treatments can reach patients more quickly.

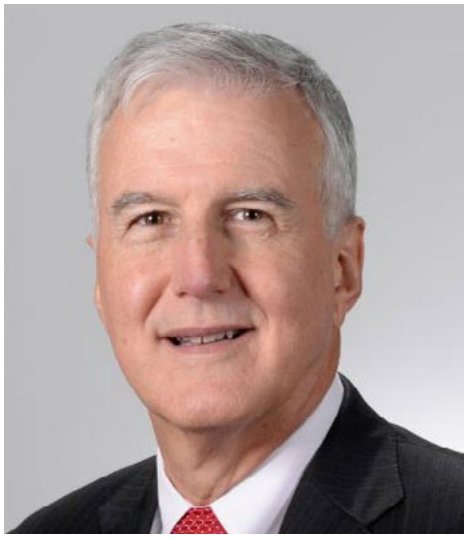
## REGISTER NOW

*A detailed program agenda, speaker list, and additional descriptions of pre- and post- workshop activities are available at the website:*

**https://aaadv.org/**

IN BRIEF


# William Cance named interim director of University of Arizona Cancer Center as Andrew Kraft steps down



William Cance, deputy director of the University of Arizona Cancer Center in Phoenix, was appointed interim director of the UA Cancer Center, effective July 1.

Cance's appointment was announced April 16 in an email from Michael D. Dake, senior vice president, UA Health Sciences. On March 28, Andrew S. Kraft, the cancer center director, said he would be stepping down from that position.

*The text of Drake's email follows:*

Dr. Cance is a renowned oncology surgeon and physician-scientist who joined the UA in October 2016. He holds the position of professor, Departments of Interdisciplinary Oncology, Pharmacology & Toxicology, and Surgery for the UA Colleges of Medicine and Pharmacy–Phoenix. Dr. Cance received his medical degree from Duke University. He completed his residency in general surgery at Barnes Hospital/Washington University School of Medicine and a fellowship in surgical oncology at Memorial Sloan Kettering Cancer Center.

Dr. Cance is the principal investigator on a 25-year R01 grant from the National Cancer Institute (NCI) focusing on focal adhesion kinase (FAK). He has been awarded numerous other grants from the NCI and National Institutes of Health, as well as the American Cancer Society, Susan G. Komen Breast Cancer Foundation and the U.S. Department of Defense. He has served on the NCI Board of Scientific Counselors and is currently a member of NCI Subcommittee F that focuses on institutional training and education. His cancer focus and expertise includes thyroid cancer, parathyroid disease, advanced GI malignancies and he is board-certified in general surgery.

Since his arrival, he has made enormous strides in Phoenix and across the state to establish a culture of collaboration to advance cancer care and treatment. He will oversee all clinical operations and research for the UA Cancer Center and will have a primary leadership role in the UA Cancer Center's 2020 submission for renewal of our Cancer Center Support Grant.

I am confident that his keen focus on collaboration will enhance programs, advance basic science, reduce disparities and elevate the UA Cancer Center's reputation for excellence in service to our state.

*The text of Kraft's email follows:*

Dear Colleagues,

I want to let you know that I will be stepping down as Director of the University of Arizona Cancer Center effective June 30th. I would like to thank you for your efforts in building cancer research at the UACC and impacting on our patients. Since I arrived, together we have accomplished much in the last 4 ½ years including obtaining National Cancer Institute designation, developing a new External Advisory Board and Community Advisory Committee, solidifying program leadership, building shared resources, and developing a strong clinical component to our Cancer Center. Together, we have started a new Human Immune Monitoring Facility, a CRISPR-Cas9 Gene Editing Service, a Bioinformatics Shared Resource, and a Drug Discovery Core at UACC-Phoenix. Having recruited national leaders in Outreach and Engagement, Immunobiology, and Head and Neck Cancer, we have strengthened the foundation of the UA Cancer Center. I know that the future is bright, and I look forward to working with each of you as a faculty member at UA.

## Jefferson, Temple extend due diligence period for negotiations over sale of Fox Chase

Thomas Jefferson University and Temple University have agreed on a 90-day extension of the due diligence period for the purchase of Temple-owned Fox Chase Cancer Center.

"We are having extensive and productive discussions with Temple leadership about Fox Chase Cancer Center and how best to work together to make healthcare more accessible to everyone in Philadelphia," Steve Klasko, president of Thomas Jefferson University and CEO of Jefferson Health, said in a statement. "The complexity and importance of the transaction requires additional time for assessment."

On Jan. 10, the parties agreed on a 90-day due diligence period (The Cancer Letter, Jan 18). Now, the deadline has been extended to June 30.

No cancer center carrying an NCI designation has ever been sold on open market. Fox Chase, which has the highest level of NCI designation—that of a comprehensive cancer center—was sold to Temple in 2012 for $84 million. Jefferson has the NCI Cancer Center designation.

Any agreement Jefferson and Temple may reach would be subject to federal and state regulatory approval.

Not only is Fox Chase a comprehensive cancer center, but it's one of the "dedicated cancer centers," a group of 11 freestanding institutions that treat cancer and no other disease. These centers are exempt from being reimbursed based on DRGs, or Diagnosis-Related Groups, under the Prospective Payment System.

The deal, as originally discussed, also included the sale of Temple's interest in Health Partners Plans, a Philadelphia-based HMO that serves Medicare, Medicaid and Children's Health Insurance Program populations in the state.

Jefferson is a rapidly growing health system that has 14 sites in downtown Philadelphia, Northern and Northeastern Philadelphia, and South Jersey. The system also has 20 network affiliates.

## Dany Habr named chief medical officer at Pfizer Oncology

Dany Habr has joined Pfizer Oncology as chief medical officer as of April 15.

Habr joins Pfizer from AbbVie where he served as their head of Oncology Global Medical Affairs, where he led launch readiness for medicines in hematology, lung and brain cancer indications. Prior to that he was the Global Clinical Development head for medicines to treat myelofibrosis, multiple myeloma, lung and breast cancer at Novartis.

"Dr. Habr's experience is unparalleled in the industry and he has a strong passion for oncology. We are delighted to have him join the team as we continue on our path of developing the best possible treatment options for cancer patients," Andy Schmeltz, Global President and General Manager, Pfizer Oncology, said in a statement.

Habr replaces Charles Hugh-Jones, who left Pfizer for Allergan last summer.

Earlier this year, Mace Rothenberg was promoted from his position as chief development officer, oncology, to chief medical officer.

## Lisa Kachnic named chair of Columbia Department of Radiation Oncology, chief of Radiation Oncology Service at NY-Presbyterian/ Columbia University Irving Medical Center

Lisa Kachnic was named chair of the Department of Radiation Oncology at the Columbia University Vagelos College of Physicians and Surgeons and chief of the radiation oncology service at New York-Presbyterian/Columbia University Irving Medical Center effective

Sept. 1. She will also serve as associate director for Cancer Network Strategy in the Herbert Irving Comprehensive Cancer Center.

Kachnic is currently a professor and chair of the Department of Radiation Oncology at the Vanderbilt University School of Medicine. She previously served on the radiation oncology faculty at Massachusetts General Hospital and Boston University School of Medicine. She is a fellow of the American Society for Radiation Oncology.

A past president and current governor of the American Board of Radiology, Kachnic is the vice chair of the radiation oncology committee and co-chair of the ano-rectal subcommittee for the SWOG Cancer Research Network research base, where she serves as the multi-modality executive officer. Kachnic is also the chair of the NRG Oncology, NCI Community Oncology Research Program's Cancer Control and Prevention Division, and is involved in NRG Oncology's GI strategic committee.

## ASCO & The Conquer Cancer Foundation announce merit awards

The Conquer Cancer Foundation of the American Society of Clinical Oncology announced the recipients of its 2019 ASCO Annual Meeting Merit Awards. These awards support oncology trainees who are first authors on abstracts selected for presentation at the ASCO annual meeting.

This year, Conquer Cancer recognized 125 recipients with Merit Awards at the 2019 ASCO Annual Meeting, having already awarded 33 symposia-specific Merit Awards in 2019. These oncology professionals are recognized for their respective field and research advancements within the cancer care community.

The complete list of 2019 ASCO Annual Meeting Merit Award is posted here.

Special Merit Awards are presented each year to trainees and junior faculty who have the top-ranking abstracts for the ASCO Annual Meeting. The ASCO Scientific Program Committee will present five additional recipients with Special Merit Awards in their respective abstract categories:

- **Dai Chihara**, NCI at NIH
  - Receives the Bradley Stuart Beller Endowed Merit Award for the highest ranking abstract overall.
  - Supported by Friends and Family of Dr. and Mrs. Ronald Beller.
- **Sarah Abou Alaiwi**, Dana-Farber Cancer Institute
  - Receives the Allen S. Lichter, MD, Endowed Merit Award for the second highest ranking abstract overall.
- **Po-Ju Lin**, University of Rochester Medical Center
  - Receives the Pain and Symptom Management Special Merit Award for the highest ranked abstract in pain and symptom management research.
- **Adriana Fonseca**, The Hospital for Sick Children
  - Receives the Brigid Leventhal Special Merit Award for the top-ranking abstract in pediatric oncology.
  - Supported by The Berry Family.
- **Sumit Gupta**, The Hospital for Sick Children
  - Receives the James B. Nachman Endowed ASCO Junior Faculty Award in Pediatric Oncology for the highest scoring abstract in pediatric oncology.
  - Supported by Friends and Family of Dr. James B. Nachman.

## IMF co-founders Susie and Brian Durie receive honorary doctorate from Vrije Univesiteit Brussel

International Myeloma Foundation co-founder and president, Susie Durie, and Chairman Brian Durie were awarded a joint honorary doctorate for scientific excellence from the Vrije Universiteit Brussel at a ceremony in Brussels.

Honorary doctorates were also bestowed upon Swedish statistician Hans Rosling (given posthumously), French mathematics historian Karine Chemla, Belgian pioneering mathematician Freddy Van Oystaeyen, American mathematician and champion of better STEM education Padmanabhan Seshaiyer, Dutch physicist and science communicator Robbert Dijkgraaf, and political cartoonist Gerard Alsteens.

The university praised what its leadership called Durie's "extraordinary" merit: "He is at the foundation of the development of new diagnostic and therapeutic possibilities, which have led to a significant increase in life expectancy following the diagnosis of multiple myeloma." Together with Susie Durie, they founded the IMF "to inform patients and to involve them in the knowledge about their illness, but also to encourage doctors worldwide to work together to develop best practice guidelines."

## Margo Shoup to join Western Connecticut Health Network as network chair of cancer service line

Western Connecticut Health Network has announced the appointment of Margo Shoup as the new network chair of the cancer service line. Shoup will provide strategic and clinical leadership for all aspects of WCHN's cancer services, including medical oncology and subspecialty practices.

In her role as network chair, Shoup will oversee the integration of cancer services, especially as WCHN forms a new, unified innovative health system with Health Quest, to be called Nuvance Health. Cancer services include diagnostic imaging, genetic counseling, medical oncology, radiation oncology, surgical oncology, research and clinical trials, and support services.

Shoup will also develop multidisciplinary disease management teams. Specialists and services dedicated to specific types of cancer will wrap around patients. Patients will have the most advanced and expert diagnoses, treatments, and care plans delivered expeditiously and conveniently in the same health network.

Shoup will also manage the first-of-its-kind cancer care collaboration with Memorial Sloan Kettering Cancer Center that successfully launched at Norwalk Hospital in 2017. The aim of the unique collaboration is to accelerate access to the newest cancer treatments for residents of Fairfield County, Connecticut. To learn more about MSK physicians at Norwalk Hospital visit MSKatNorwalk.org.

Shoup currently serves as president of the Central Surgical Association, and treasurer of the Western Surgical Association. She is also a member of the Society for Surgical Oncology, the Society of University Surgeons, and the Southern Surgical Association.

From 2012 to 2018, she was a director of the American Board of Surgery, as the representative for the American College of Surgeons.

THE CANCER LETTER | APRIL 19, 2019 | VOL 45 | ISSUE 16

# THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

## ACP screening guidance calls for two-year interval between mammograms for women at average breast cancer risk

Average-risk women, between the ages of 50 and 74, who have no symptoms for breast cancer should undergo breast cancer screening with mammography every other year, the American College of Physicians states in a new evidence-based guidance statement published today in Annals of Internal Medicine.

The guideline can be published here.

ACP's guidance statement does not apply to patients with prior abnormal screening results or to higher risk populations, such as women with a personal history of breast cancer or a genetic mutation known to increase risk.

"Beginning at age 40, average-risk women without symptoms should discuss with their physician the benefits, harms, and their personal preferences of breast cancer screening with mammography before the age of 50," ACP president Ana María López said in a statement. "The evidence shows that the best balance of benefits and harms for these women, which represents the great majority of women, is to undergo breast cancer screening with mammography every other year between the ages of 50 and 74."

Every other year mammography screening results in no significant difference in breast cancer mortality while substantially reducing screening harms when compared to annual screening. Women screened annually receive more abnormal results that do not represent an actual breast cancer diagnosis than women screened every other year (7.0% vs. 4.8%). These false-positive findings result in biopsies and surgeries that would otherwise not have been necessary.

About 20% of women diagnosed with breast cancer over a 10-year period will be overdiagnosed and likely overtreated. Overdiagnosis means a woman is diagnosed with a breast cancer that would not have made her sick or led to her death if not diagnosed or treated. Therefore, finding this cancer is not of clinical benefit to the woman.

Harms of breast cancer screening include false positive results (from a test showing an abnormality even though the woman does not have breast cancer), overdiagnosis, overtreatment, radiation exposure, and radiation associated breast cancers and breast cancer deaths, as well as worry and distress from tests and procedures including breast biopsies.

Recommended strategies vary for breast cancer screening in average-risk women. The age to start and discontinue mammography, screening intervals, the role of imaging methods other than mammography, and the role of clinical breast examination have been points of disagreement among guideline developers.

Rather than developing a new clinical practice guideline in these circumstances ACP instead prepares and releases guidance statements that rely on evidence presented or referenced in selected guidelines and accompanying evidence reports. ACP guidance statements do not include new reviews or searches of the literature outside the body of evidence referenced by the reviewed guidelines.

In "Screening for Breast Cancer in Average-risk Women," ACP reviewed guidelines from the American College of Radiology, American Cancer Society, American College of Obstetricians and Gynecologists, the Canadian Task Force on Preventive Health Care, the National Comprehensive Cancer Network, the United States Preventative Services Task Force, and the World Health Organization.

## Artificial intelligence performs as well as experienced radiologists in detecting prostate cancer

UCLA researchers have developed a new artificial intelligence system to help radiologists improve their ability to diagnose prostate cancer. The system, called FocalNet, helps identify and predict the

aggressiveness of the disease evaluating magnetic resonance imaging, or MRI, scans, and it does so with nearly the same level of accuracy as experienced radiologists.

In tests, FocalNet was 80.5% accurate in reading MRIs, while radiologists with at least 10 years of experience were 83.9% accurate.

The research is published online in IEEE Transactions on Medical Imaging. The paper was presented at the IEEE International Symposium on Biomedical Imaging in April 2019 and was selected as the runner up-for best paper.

The paper can be found here.

FocalNet is an artificial neural network that uses an algorithm that comprises more than a million trainable variables; it was developed by the UCLA researchers. The team trained the system by having it analyze MRI scans of 417 men with prostate cancer; scans were fed into the system so that it could learn to assess and classify tumors in a consistent way and have it compare the results to the actual pathology specimen. Researchers compared the artificial intelligence system's results with readings by UCLA radiologists who had more than 10 years of experience.

The research suggests that an artificial intelligence system could save time and potentially provide diagnostic guidance to less-experienced radiologists.

The study's senior authors are Kyung Sung, assistant professor of radiology at the David Geffen School of Medicine at UCLA; Steven Raman, a UCLA clinical professor of radiology and a member of the UCLA Jonsson Comprehensive Cancer Center; and Dieter Enzmann, chair of radiology at UCLA. The lead author is Ruiming Cao, a UCLA graduate student. Other authors are Amirhossein Bajgiran, Sohrab Mirak, Sepideh Shakeri and Xinran Zhong, all of UCLA.

The work was supported by funds from the Integrated Diagnostics Program, Department of Radiological Sciences & Pathology, David Geffen School of Medicine at UCLA.

## Mount Sinai launches clinical trial of new imaging device for head and neck cancer surgeries

Mount Sinai Health System has launched a clinical trial of a new imaging device for detecting head and neck cancer during surgery.

The device, called Otis Wide Field OCT, by Perimeter Medical Imaging, is an ultra-high-resolution imaging system that can image tumor specimens in real time during surgery, allowing surgeons to remove all of the cancerous tissue during one procedure, rather than waiting for traditional pathology results to come in afterward, which can often lead to additional procedures.

Patients in the trial agree to have their tumors placed in the system for imaging, which is then compared to the standard pathology evaluation.

"State-of-the-art imaging platforms, such as the Otis system and others, will likely play a significant role in the future of head and neck cancer surgery. While traditional pathologic examination of tissues is the standard around the world, we need new technology to allow us to detect cancer and ensure adequate resection at the time of surgery," explains lead investigator Brett Miles, associate professor of Otolaryngology at the Icahn School of Medicine at Mount Sinai, and co-chief of the Division of Head and Neck Oncology for the Mount Sinai Health System.

"Data from this study, and other projects in the optical imaging program, will help us understand how beneficial these technologies may be and drive future innovation during head and neck cancer surgery," Miles said in a statement.

Men's risk of contracting these cancers is twice as high as women's. Tobacco use and excessive drinking are major contributors, especially for male patients over the age of 50. However, cancers of the oropharynx are dramatically increasing among younger men who don't smoke, because of the human papillomavirus.

The U.S. Centers for Disease Control and Prevention estimates that more than 16,000 HPV-associated oropharyngeal cancers are diagnosed yearly in the United States, while The American Cancer Society says 7% of adult Americans have oral HPV. Men are four times more likely to develop these cancers than women, and this ratio may nearly double by 2030.

"Although no screening test currently exists for early detection of HPV-related oropharyngeal cancers, it is critically important to recognize symptoms of the disease. Any patient with persistent throat pain or a lump in the neck needs to be evaluated by a physician," Raymond Chai, assistant professor of Otolaryngology at the Icahn School of Medicine at Mount Sinai, and director of Head and Neck Robotic Surgery at Mount Sinai Downtown said.

"The FDA has recently approved the expansion of Gardasil 9, the HPV vaccine, for use in patients from the ages of 27 to 45. The vaccine has been previously demonstrated to prevent over 90% of possible HPV-related cancers," Chai said in a statement.

Investigators from the Head and Neck Cancer Research Program at the Icahn School of Medicine at Mount Sinai are also conducting a high-risk HPV screening study, along with colleagues from

Johns Hopkins University and three other institutions.

The study, known as MOUTH, is a clinical trial to better understand how risk factors affect oral HPV infection rates. In this study, researchers are collecting samples of blood, saliva, and urine to test them for HPV antibodies.

So far, approximately 630 samples have been collected, and patients who screened positive for high-risk HPV viral types are entering the close observational arm of the study, in which they will receive clinical visits and imaging, such as ultrasound and MRI, to monitor them for head and neck cancer. They will be monitored annually for the next five years. The study is currently open and enrolling patients.

## Cervical cancer subtype rising in some sub-populations

A new study reports that a type of cervical cancer that is less amenable to Pap testing is increasing in several subpopulations of women, pointing to the growing importance of human papillomavirus testing and vaccination. The study can be found here.

Overall trends in cervical cancer incidence have been driven by declines in squamous cell carcinoma, which account for the majority of cervical cancers. Most of the rest are adenocarcinomas, for which Pap testing is less sensitive.

While overall cervical cancer rates have been dropping for decades, cervical adenocarcinomas seem to have become more common in the past 20 to 30 years. But there has been limited reporting on recent trends.

To learn more, investigators led by Farhad Islami, analyzed recent cervical cancer incidence trends by histology and age in the U.S. They examined trends in squamous cell carcinoma and adenocarcinoma incidence rates in the U.S. by age group, race/ethnicity, and stage at diagnosis using data from the U.S. Cancer Statistics Incidence Analytic Database.

They found squamous cell carcinoma incidence rates continued to decrease in all racial/ethnic groups except among non-Hispanic whites, in whom rates stopped dropping in the 2010s. For adenocarcinoma, after being stable between 1999 and 2002, incidence rates among non-Hispanic whites rose 1.3% per year during 2002–2015.

Those increases were driven by steeper increases in women ages 40 to 49, among whom cervical adenocarcinoma rates rose 4.4% per year since 2004, and women 50 to 59 years, among whom rates rose 5.5% per year since 2011. Adenocarcinoma incidence decreased in blacks and Hispanics during 1999–2015 and was stable in Asian/Pacific Islanders.

"Increasing or stabilized incidence trends for [adenocarcinoma] and attenuation of earlier declines for [squamous cell carcinoma] in several subpopulations underscore the importance of intensifying efforts to reverse the increasing trends and further reduce the burden of cervical cancer in the U.S.," the study said.

The authors state that "more efforts are needed to increase screening utilization according to guidelines and appropriate follow-up of positive results" to further reduce the burden of cervical cancer.

They note that increasing the use of HPV testing may improve early detection of adenocarcinoma, but they also recommend research to further improve screening strategies to reduce overdiagnosis, which may be more common with HPV testing. HPV vaccination is an effective tool to prevent cervical cancer because virtually all these cancers are caused by HPV infection.

DRUGS & TARGETS

# FDA approves Balversa for urothelial carcinoma with FGFR genetic alterations

Janssen Pharmaceuticals said Balversa (erdafitinib) received accelerated approval from FDA for the treatment of adults with locally advanced or metastatic urothelial carcinoma which has susceptible fibroblast growth factor receptor 3 or FGFR2 genetic alterations and who have progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Balversa is the first FGFR kinase inhibitor approved by FDA. The accelerated approval follows FDA Breakthrough Therapy Designation in March 2018 and Priority Review Designation of the New Drug Application submitted in September 2018.

Balversa, a once-daily oral FGFR kinase inhibitor, received accelerated approval based on results from a phase II clinical trial (BLC2001, NCT02365597), a multicenter, open-label, single-arm study, of 87 patients with disease that had progressed on or after at least one prior chemotherapy and that had at least one of the following genetic alterations: FGFR3 gene mutations (R248C, S249C, G370C, Y373C) or FGFR gene fusions (FGFR3-TACC3, FGFR3-BAIAP2L1, FGFR2-BICC1, FGFR2-CASP7), as determined by a clinical trial assay performed at a central laboratory.

The results demonstrated a 32.2% objective response rate as assessed by Blinded Independent Review Committee [95% CI (22.4, 42.0)]. Responders included patients who had previously not responded to anti PD-L1/PD-1 therapy.

In the trial, ORR was defined as the percentage of patients with measurable lesions achieving a complete response [2.3%] or partial response [29.9%] to treatment using the Response Evaluation Criteria in Solid Tumors Version 1.1 criteria, a standard way to measure how well a patient responds to treatment based on whether tumors shrink, stay the same, or get bigger as assessed per investigator.

Results also showed a median duration of response of 5.4 months [95% CI (4.2, 6.9)] in patients treated with Balversa. There were no confirmed responses to Balversa in the FGFR2 fusion patient population (n=6). Data from the BLC2001 study were presented at the ASCO 2018 Annual Meeting (Abstract #4503) and were recognized as a "Best of ASCO" selection.

FDA simultaneously approved a companion diagnostic for use with Balversa, the QIAGEN therascreen FGFR RGQ Reverse-transcription-polymerase chain reaction Kit, which is the first PCR-based companion diagnostic approved to detect FGFR alterations.

The therascreen FGFR test detects the presence of FGFR alterations in the tumor tissue of patients with mUC. If one or more of the genetic alterations or fusions are detected, the patient may be a candidate for treatment with Balversa.

Balversa (erdafitinib) is a once-daily, oral fibroblast growth factor receptor kinase inhibitor indicated for the treatment of adults with locally advanced or metastatic urothelial carcinoma which has susceptible FGFR3 or FGFR2 genetic alterations and who have progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

In 2008, Janssen entered into an exclusive worldwide license and collaboration agreement with Astex Pharmaceuticals to develop and commercialize Balversa. Balversa will be commercially available through the single-source specialty pharmacy provider US Bioservices.

# FDA expands pembrolizumab indication for first-line treatment of NSCLC

FDA has approved pembrolizumab (Keytruda) for the first-line treatment of patients with stage III non-small cell lung cancer who are not candidates for surgical resection or definitive chemoradiation or metastatic NSCLC. Patients' tumors must have no EGFR or ALK genomic aberrations and express PD-L1 (Tumor Proportion Score ≥1%) determined by an FDA-approved test.

Keytruda is sponsored by Merck.

Pembrolizumab was previously approved as a single agent for the first-line treatment of patients with metastatic NSCLC whose tumors express PD-L1 TPS ≥50%.

Approval was based on KEYNOTE-042 (NCT02220894), a randomized, multicenter, open-label, active-controlled trial conducted in 1274 patients with stage III or IV NSCLC who had not received prior systemic treatment for metastatic NSCLC and whose tumors expressed PD-L1 (TPS ≥1%). PD-L1 expression was determined by an immunohistochemistry assay using the PD-L1 IHC 22C3 pharmDx Kit.

Patients were randomized (1:1) to receive pembrolizumab 200 mg intravenously every 3 weeks or investigator's choice of a carboplatin-containing regimen with either pemetrexed or paclitaxel. Randomization was stratified by ECOG performance status, histology, geographic region, and PD-L1 expression (TPS ≥50% vs. TPS 1 to 49%).

Overall survival in the TPS ≥50% NSCLC subgroup, the TPS ≥20% NSCLC subgroup, and the overall population (TPS ≥1%) were the major efficacy measures. The trial demonstrated statistically significant OS improvements for those randomized to pembrolizumab compared with chemotherapy in all three populations.

In the TPS ≥1% population (overall population), the median OS was 16.7 and 12.1 months for the pembrolizumab and chemotherapy arms, respectively (HR 0.81; 95% CI: 0.71, 0.93; p=0.0036).

For the TPS ≥ 20% subgroup, the median OS was 17.7 months for the pembrolizumab arm and 13.0 months for the chemotherapy arm (HR 0.77; 95% CI: 0.64, 0.92; p=0.004). For the TPS ≥50% subgroup, the estimated median OS was 20 months and 12.2 months for those receiving pembrolizumab and chemotherapy, respectively (HR 0.69; 95% CI: 0.56, 0.85; p=0.0006).

There were no significant differences in progression-free survival or overall response rate between arms in any population.

## Aprea Therapeutics receives FDA Fast Track and Orphan Drug designations for APR-246 for MDS

Aprea Therapeutics said FDA has granted Fast Track designation to APR-246 for the treatment of patients with MDS having a TP53 mutation. In addition, FDA has also granted Orphan Drug Designation to APR-246 for treatment of MDS.

The FDA's Fast Track program facilitates the development of drugs intended to treat serious conditions and that have the potential to address unmet medical needs. A drug program with Fast Track status is afforded greater access to the FDA for the purpose of expediting the drug's development, review and potential approval.

In addition, the Fast Track program allows for eligibility for accelerated approval and priority review, if relevant criteria are met, as well as for Rolling Review, which means that a drug company can submit completed sections of its New Drug Application for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be submitted for review.

The p53 tumor suppressor gene is the most frequently mutated gene in human cancer, occurring in approximately 50% of all human tumors. These mutations are often associated with resistance to anti-cancer drugs and poor overall survival, representing a major unmet medical need in the treatment of cancer.

APR-246 has been shown to reactivate mutant and inactivated p53 protein—by restoring wild-type p53 conformation and function—and thereby induce programmed cell death in human cancer cells. APR-246 has demonstrated pre-clinical anti-tumor activity in a wide variety of solid and hematological tumors, including MDS, AML, and ovarian cancer, among others.

Additionally, strong synergy has been seen with both traditional anti-cancer agents, such as chemotherapy, as well as newer mechanism-based anti-cancer drugs and immuno-oncology checkpoint inhibitors. In addition to pre-clinical testing, a Phase I/II clinical program with APR-246 has been completed, demonstrating a favorable safety profile, biological activity and clinical responses in hematological malignancies and solid tumors with mutations in the TP53 gene.

## Intensity Therapeutics receives Fast Track designation for development of INT230-6 in breast cancer

Intensity Therapeutics Inc. said FDA has granted Fast Track designation to the company's development program evaluating INT230-6 for the treatment of patients with relapsed or metastatic triple negative breast cancer who have failed at least two prior lines of therapy.

Approximately 15-20% of breast cancers test negative for estrogen receptors, progesterone receptors, and excess HER2 protein, qualifying them as triple negative. According to a study published in the Journal of Clinical Oncology, patients who fail two lines of therapy for TNBC typically progress within nine weeks. Those who have failed three lines progress within four weeks.

INT230-6, Intensity's lead product candidate designed for direct intratumoral injection, is comprised of two proven, potent anti-cancer agents and a penetration enhancer molecule that helps disperse the drugs throughout tumors and diffuse into cancer cells.

INT230-6 is being evaluated in a phase I/II clinical study (NCT03058289) in patients with various advanced solid tumors. In preclinical studies, INT230-6 eradicated tumors by a combination of direct tumor kill and recruitment of dendritic cells to the tumor micro-environment that induced anti-cancer T-cell activation.

Treatment with INT230-6 in in vivo models of severe cancer resulted in substantial improvement in overall survival compared to standard therapies. Further, INT230-6 provided complete responder animals with long-term, durable protection from multiple re-inoculations of the initial cancer and resistance to other cancers. In mouse models, INT230-6 has shown strong synergy with checkpoint blockage, including anti-PD-1 and anti-CTLA4 antibodies. INT230-6 was discovered from Intensity's DfuseRxSM platform.

## Kitov announces milestone in FameWave acquisition

Kitov Pharma Ltd. announced a milestone in the acquisition of FameWave Ltd., following signature of a clinical collaboration agreement between FameWave and Bristol Myers Squibb for their planned phase I/II clinical trials to evaluate the combination of CM-24, a monoclonal antibody targeting the novel immune checkpoint carcinoembryonic antigen-related cell adhesion molecule 1 with nivolumab in patients with non-small cell lung cancer.

Preclinical studies have shown a strong synergetic anti-cancer effect using CM-24 in combination with a PD-1 antibody. Based on Kitov's review of the initial phase I dose ranging study of CM24 as a single agent, performed by Merck Sharpe & Dohme, Kitov plans to explore higher doses in order to reach receptor saturation,.

Kitov is acquiring FameWave, pending completion of certain additional closing conditions, including approval by the shareholders of Kitov of the acquisition.

CM-24 is a humanized monoclonal antibody directed against carcinoembryonic antigen-related cell adhesion molecule 1, an immune checkpoint protein belonging to the Human CEA protein family. Evidence has shown that CEACAM1 is expressed on tumor lymphocytes and is up-regulated in several cancer types.

Preclinical studies have shown evidence that CM-24 enhances the cytotoxic activity of tumor-infiltrating lymphocytes against various CEACAM1-positive tumor cell lines. CM-24 is being developed for multiple oncological indications according to the expression pattern of its target protein.

As part of the recently announced agreement for the acquisition of FameWave by Kitov, cCAM BioTherapeutics Ltd., a wholly owned subsidiary of Merck Sharp and Dohme Corp., known as "MSD" in Israel, has returned the rights to CM-24 to former cCAM shareholders and founders of FameWave, following an initial phase I dose ranging study of CM-24 as single agent.

## Stanford partners with Notable and Tempus to make rapid personalized treatment in blood cancer patients

Notable and Stanford Medical Center announced the results of a new study on the feasibility of personalized medicine. The study's objective was to rapidly sequence MDS blood cancer samples; analyze each sample against hundreds of drugs and drug combinations; and make personalized treatment recommendations for each sample—all within a maximum of 30 days.

Twenty patients were represented in the study, and Stanford/Notable were able to complete their personalized recommendations within Stanford's target of 30 days for all 20 patients. With respect to accuracy, interim clinical data demonstrated both positive and negative predictive value average of 84%.

Effective treatment and time-to-treatment are both essential elements of fighting cancer. Advances in personalized medicine now make it possible to analyze samples for individual patients and point physicians and patients towards the drugs and drug combinations that are likely to be most effective for their unique cancer. This technique has the potential to drastically improve the way physicians treat cancers, and save more lives.

Steps involved in the study:

1. Stanford Medical Center sent the blood samples to Notable and Tempus;
2. Notable analyzed hundreds of requested drugs and drug combos against each sample; Tempus did the DNA sequencing;
3. The Stanford MDS tumor board combined data for each patient into a report; and
4. The report and personalized treatment recommendation was then shared with physician for each patient.

"Ex vivo drug sensitivity technology must have a rapid turnaround time, accuracy and efficacy in order to be useful in the clinic," said Peter Greenberg, professor of medicine (hematology) and director of Stanford MDS Center at Stanford University Cancer Center, said in a statement.

"Notable Lab's ex vivo drug sensitivity assay screened marrow samples we sent them from patients in our recent biologically focused feasibility trial against a collection of investigational and FDA-approved compounds," Greenberg said. "These patients had higher risk myelodysplastic syndromes and were refractory to standard therapy. Potentially actionable therapeu-

tic results were returned to us for the patients enrolled in our trial within a clinically actionable time frame. These data suggest the potential utility of this methodology to aid in decision-making for novel therapeutic drug selection in MDS patients with HMA-refractory disease."

Further data regarding the trial and methodology used will be presented at the upcoming European Hematology Association annual meeting hosted in Amsterdam in June.

Founder Matt De Silva started the company when his own father was suffering from a deadly brain cancer—his goal was to find a way to help physicians quickly match patients with the most effective treatments. "This partnership represents the future of precision medicine because it combines the strength of molecular sequencing with next-generation functional drug sensitivity tests," said De Silva. "It's the type of trial I wish had existed for my dad because these approaches produce immediately actionable treatment options for physicians and their patients."

Stanford Medical Center, Notable and Tempus are working to prepare a detailed paper on the study's approach and results, for publication later this year.

## OncoSec anounces collaboration with Duke to study TAVO + plasmid DNA vaccines in breast cancer

OncoSec Medical Inc. and Duke University School of Medicine said they have entered into a collaborative research agreement to evaluate the use of OncoSec's proprietary TAVOPLUS (enhanced IL-12 DNA-plasmid) in combination or sequence with a HER2-plasmid vaccine administered with OncoSec's novel intratumoral delivery system.

The research will be led by Herbert Kim Lyerly, George Barth Geller Professor, Professor of Immunology, Surgery and Pathology at Duke University School of Medicine.

"We are eager to expand our immunotherapy research in breast cancer through this collaboration with OncoSec. We have previously demonstrated, in a variety of breast cancer models, that local delivery of IL-12 stimulates an anti-breast cancer immune response with applicability beyond end-stage cancer," Lyerly said in a statement.

"This delivery system has the potential to be a foundational therapeutic in the treatment of early-stage disease. The translational work with TAVOPLUS has been very encouraging and we are excited to explore the potential of OncoSec's IL-12 plasmid delivery technology to enhance immune responses targeting HER2+ tumors and to elicit superior T-cell and B-cell responses to HER2 in a variety of preclinical breast cancer models."

Under the agreement, OncoSec will provide its proprietary TAVO (IL-12 plasmids) and its new electroporation generator, APOLLO, using lower voltage and a longer pulse width which greatly increased DNA-plasmid cellular transfection rates, to Duke University's Center for Applied Therapeutics.

Duke investigators will conduct preclinical studies using plasmid vaccines targeting HER2 in combination with plasmid vaccines and TAVO in a newly developed endogenous mouse model of HER2+ breast cancer. Additionally, Duke investigators will use TAVO with their high-intensity ultrasound tumor ablation models to explore the impact of IL-12 delivery on the development of systemic immunity.

## Roswell Park selects Circuit Clinical as collaborator for CIMAvax clinical trial

Circuit Clinical announced a collaboration with Roswell Park Comprehensive Cancer Center to support the expansion of clinical trial opportunities to its outpatient oncology practices. This collaboration marks Circuit Clinical's entry into oncology clinical research, with both digital and clinical services.

Circuit Clinical will be delivering both research operational support and TrialScout– its patient experience platform– in support of Roswell Park's groundbreaking CIMAvax-EGF Clinical Trial.

Circuit Clinical will be providing patient identification, engagement, enrollment and ongoing patient experience support services under the direction of the Roswell Park Comprehensive Cancer Center clinical research leadership team.

In addition to its main campus on Carlton Street in the City of Buffalo, Roswell Park offers care at satellite offices in Amherst and Niagara Falls and at five affiliated community practices.

Through this collaboration, eligible patients with certain forms of lung and head/neck cancer will have the opportunity to participate in the CIMAvax Clinical Trial onsite at one or more of the following practices:

- Roswell Park Jamestown Medical Oncology & Hematology,
- Roswell Park Hematology Oncology of Niagara,
- Roswell Park Hematology Oncology Southtowns,
- Roswell Park Hematology Oncology Northtowns.