The Early Detection of Cancer Conference
October 6-8, 2020

Recapping day one

We're glad you made it to the 2020 Early Detection of Cancer Conference. We're looking forward to more eye-opening presentations, well-argued debates and networking opportunities. Before jumping back into it, here's a quick recap of day one:

Caroline Dive (University of Manchester, CRUK Manchester Institute) brought us up to speed on efforts to improve lung cancer screening by combining CT imaging with a liquid biopsy. (Her team is running an observational cohort study to test whether blood biomarkers can detect lung cancer recurrence earlier than standard of care clinical surveillance.) The field has no shortage of potential biomarkers to choose from, including: circulating tumor cells, tumor DNA, RNA, and tumor educated platelets. Progress, Dive said, will hinge on a deeper understanding of early disease biology and pre-clinical models that more accurately represent the early stages of cancer.

To that end, Anton Berns (Netherlands Cancer Institute) highlighted the promise of autochthonous tumor models, that is, tumors induced in lab animals, in which it is possible to study early tumor formation in the presence of an intact immune system. With such models, researchers can switch particular oncogenes and tumor-suppressor genes on or off in a given tissue and compare cancer development. Berns said his team's mouse models closely recapitulate the phenotype of human cancers including small cell lung cancer, and may help identify specific early biomarkers of dangerous tumors.

The first session closed with two lightning talks: Naoki Oshimori (OHSU Knight Cancer Institute) described how a mouse model of squamous cell carcinoma enabled his team's discovery of a signaling loop between tumor-initiating cells and nearby non-cancer cells that generates the niche microenvironment that is required for invasive progression and drug resistance. Jennifer Munkley (Newcastle University Biosciences Institute) gave an update on the GlycoScore blood test for prostate cancer, which looks for specific glycans (sugars that attach to proteins, lipids, and other glycans on cells). Tested in more than 600

patient samples, a three-glycan test distinguished between benign tissue and prostate cancer with high sensitivity and specificity, she said.

Reflecting on COVID-19 The COVID-19 pandemic, as in all of medicine, has posed severe challenges for cancer screening. Participants in a special panel discussion called out opportunities the pandemic has created. When it became unfeasible for patients to visit the clinic for melanoma screening, Sancy Leachman (OHSU Knight Cancer Institute) and colleagues came up with an alternative: dermatoscopes that attach to a mobile phone, which high-risk patients can borrow and transmit images of suspicious lesions. It's become a permanent option for rural patients and those who can't easily travel. For patients with throat symptoms calling for endoscopy, Rebecca Fitzgerald (Cambridge University, MRC Cancer Unit) said her center began cautiously testing an alternative: the Cytosponge, a small mesh sponge within a soluble gelatin capsule that is swallowed and retrieved to collect esophageal cells. Kevin Monahan (St. Marks Hospital) said his team learned the cost of halting colonoscopy procedures and is working to safely maintain the service for symptomatic patients even if a pandemic second wave hits hard. Jackie Shannon (OHSU Knight Cancer Institute) said the pandemic has brought wide attention to long entrenched inequalities and health disparities, perhaps enough to drive much-needed policy changes and enduring efforts to reach underserved populations.

Leveraging risk stratification Cancer screening intensity should be matched to an individual's risk of getting cancer. Jon Emery (University of Melbourne) described efforts to use genetic testing to help patients make informed decisions on colorectal cancer screening. He said it's looking feasible to start to implement genetic risk stratification in the general practice setting. In the future, results will be even better with decision support tools that include risk factors such as diet, smoking, screening history, and medication use.

Julia Hipsley-Cox (University of Oxford) and colleagues are drawing upon the UK health system's deep and detailed patient records to develop risk stratification algorithms to target cancer screening resources to people at highest risk and most likely to benefit from interventions (you can check them out at www.qcancer.org). Other tools are designed to be integrated into electronic medical record systems.

The day ended with two more lightning talks: Rebecca Landy (National Cancer Institute) noted a huge disparity in lung cancer screening guidelines: 32% of African Americans who developed lung cancer would have been eligible for CT screening, compared with 56% of whites. She showed how an individualized risk

calculator (the LYFS-CT model) can effectively eliminate this disparity. Tom Callender (University College London) presented findings on the impact of MRI prior to biopsy on age-based and risk-tailored screening for prostate cancer. Thank you for joining us. Please accept our sincere apologies for the technical challenges. Don't forget: the video library will be updated each day with recordings of the meeting sessions.

Recapping day two

We have three more sessions lined up, but first here's a recap of Wednesday.

Risk-tailored screening is a way to fit the intensity of testing to an individual's risk of getting cancer. Hilary Robbins (International Agency for Research on Cancer) focused on the job of generating evidence that will be needed to establish risk-tailored cancer screening, presenting examples from lung cancer and breast cancer. Randomized clinical trials are not the way forward, she said, given the large numbers of subjects and lengthy follow-up needed just to answer a limited number of questions in only one context.

A cancer blood test developed by GRAIL, Inc., is being evaluated for its ability to detect more than 20 types of cancer and predict tissue of tumor origin. GRAIL Vice President Eric Fung highlighted the clinical studies that have led the company to focus on DNA methylation patterns for its multi-cancer early detection test undergoing a multicenter clinical trial due for completion in early 2021.

Two lightning talks closed the session: Amelie Lutz (Stanford University) is developing an ultrasound guided molecular imaging method for detecting ovarian cancer using microbubbles that target tumor angiogenesis. Stefano Avanzini (Stanford University) is using mathematical models to estimate the size tumors must reach to become detectable by tumor DNA circulating in blood. (For lung cancer, he estimates a median tumor detection size of 2 cm, which is a 43% decrease compared with the median size of diagnosed cancers in the SEER database.)

KEYNOTE TALK

Dinah S. Singer (National Cancer Institute) began with a rundown of the NCI's response to COVID-19 pandemic, from virus-focused research initiatives to the ways the agency is flexing to support grantees. She concluded with an overview of the cancer early detection programs the agency has underway, such as the Early Detection Research Network (now focusing on AI and machine learning to

integrate omic data to find biomarkers), and The Human Tumor Atlas Network (HTAN), a massive effort to map the complex ecosystems of cancer – and pave the way for advances in prevention, early detection and treatment.

GAMBHIR HONORED WITH DON LISTWIN AWARD

Sanjiv Sam Gambhir was an internationally recognized pioneer in molecular imaging who dedicated his career to developing methods of early disease detection. The director of the Canary Center at Stanford died of cancer on July 18. He was honored with the Don Listwin Award in a ceremony with heartfelt and moving remembrances from Utkan Demirci (Stanford University) and Iain Foulkes (Cancer Research UK). The Listwin Award was established last year to recognize a sustained contribution to, or singular achievement in, the cancer early detection field. The award is named in honor of Don Listwin, founder and chairman of the Canary Foundation.

Recap of the final day

The third and final day kicked off with some eye-opening updates from the world of AI and machine learning.

Lily Peng and Sunny Jansen (Google Health) expounded on three overlooked requirements for building successful AI models: data of high quality, not just quantity; human-centered usability, not just model accuracy; cost-effectiveness, not just excellent performance.

AI systems are becoming adept at reading radiology images and pathology slides to correctly classify lesions as cancer or benign. Parag Mallick (Stanford University) explained how tools such as saliency mapping are making it possible to understand how the machines reach their conclusions – building confidence and potentially revealing biological insights. He also showed examples of AI tools for biomarker discovery that extract and create knowledge from massive, unstructured data sets.

Two lightning talks concluded the session: Freya Woods (Swansea University) showed how AI can improve the sensitivity and specificity of cancer detection by Raman spectroscopy, which her group is developing as a triage tool in the diagnosis of colorectal cancer. Rawen Kader (University College London) and colleagues have developed a neural network to assist real time decision-making during colonoscopy by classifying polyps as pre-cancerous or not, with a randomized clinical trial in the offing.

GREAT DEBATES

Should genomic risk stratification be part of early detection? Gareth Evans (Manchester University) made the case that it must, noting that polygenic risk scores robustly predict risk for several common cancers and can be used to fit the intensity of screening to a person's risk of getting cancer. Cristian Tomasetti (Johns Hopkins University) argued that, while genomic risk stratification is useful for some cancer types, many others have no known inherited factors. He asserted that the development of affordable and minimally invasive multi-cancer blood tests will reduce the need for genetic risk stratification. Before the debate, 60% of meeting attendees agreed with Evans, and 40% agreed with Tomasetti. The ratio shifted to 50:50 after.

Before approving new early detection approaches for clinical use, should we require evidence of a cancer-specific mortality benefit from at least two randomized controlled trials? Harry De Koning (Erasmus University Medical Centre) pointed to the conflicting findings of clinical trials of screening methods such as PSA for prostate cancer to make the affirmative case. Steve Skates (Harvard University) asserted that requiring such evidence unnecessarily delays the use of early detection advances, and costs too much, when there are faster and less costly trial endpoints, such as reduction in late-stage diagnoses. In the poll of meeting attendees, agreement with De Koning dropped from 32% pre-debate to 20% percent after, with many deciding that it's too much to ask for randomized trials showing mortality benefit.

On behalf of the Canary Center at Stanford, Cancer Research UK and the OHSU Knight Cancer Institute, thank you for joining us for the 2020 Early Detection of Cancer Virtual Conference. With luck, we'll be able to meet in person at next year's meeting. For now, the organizing committee has decided to be optimistic and start preparing for an in-person gathering in London.