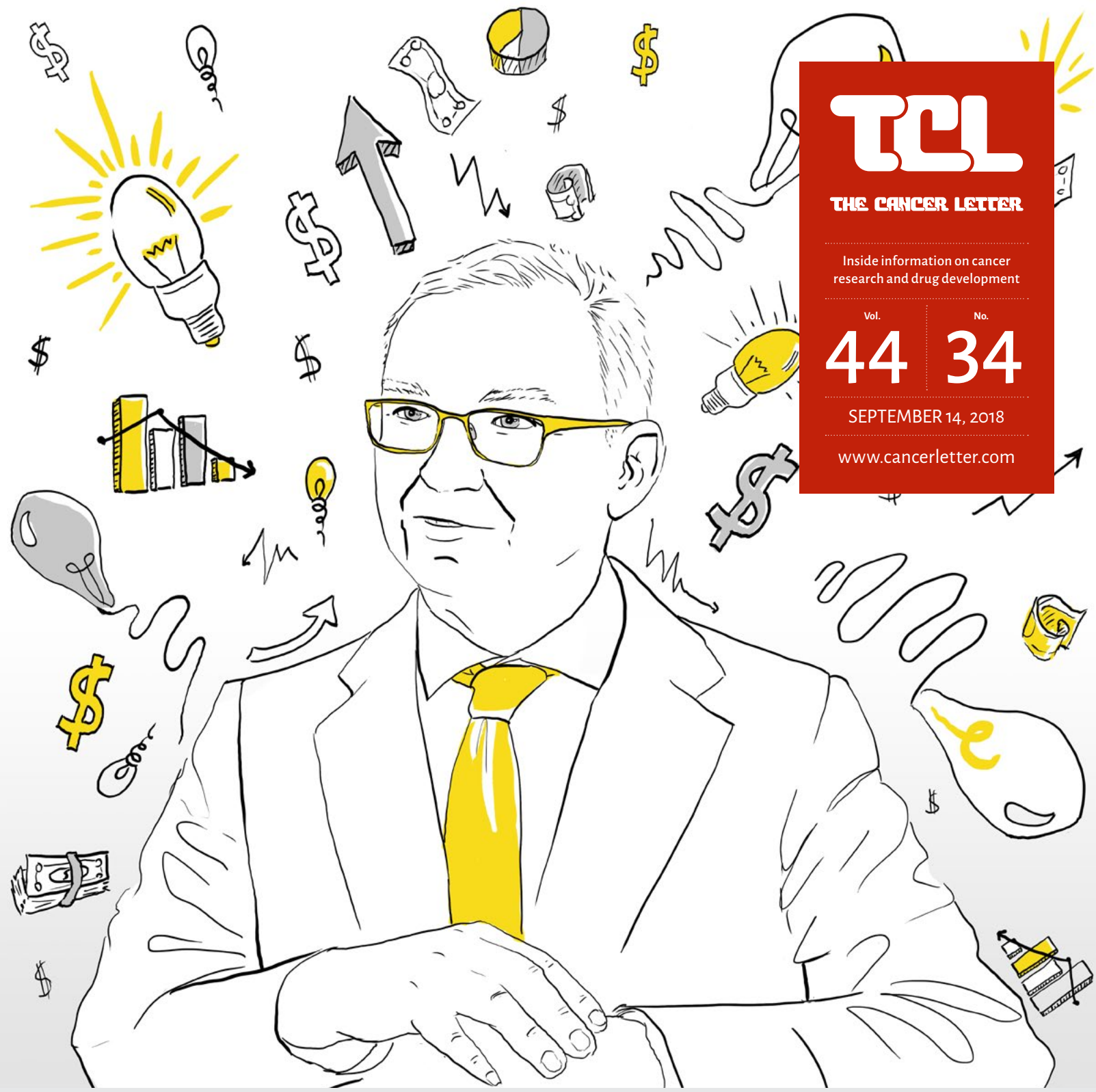

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JOSÉ BASELGA RESIGNS AS PHYSICIAN-IN-CHIEF AT MEMORIAL SLOAN KETTERING

José Baselga has resigned from his position as physician-in-chief and chief medical officer of Memorial Sloan Kettering Cancer Center less than a week after The New York Times and ProPublica reported that he had failed to disclose his conflicts of interest.

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A COLOR-CODED DOCUMENT BASELGA CREATED TO EXPLAIN HIMSELF INSTEAD ILLUSTRATED THE EXTENT OF HIS CONFUSION AND EXPOSURE

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Mays Cancer Center

UT Health San Antonio MD Anderson Cancer Center

CHIEF, Division of Hematology & Medical Oncology

The Long School of Medicine at the University of Texas Health Science Center at San Antonio (dba UT Health San Antonio) and the NCI-designated UT Health San Antonio MD Anderson Cancer Center, seeks an individual with an outstanding record of clinical activities and leadership, scientific achievement, grant support, scholarly accomplishments and mentoring as its **Chief** of the **Division of Hematology & Medical Oncology**.

The Division of Hematology & Medical Oncology plays a central role in the cancer service line developed as part of the MD Anderson Cancer Network®, and is comprised of over 20 faculty members, and over a dozen fellows in Hematology & Oncology as well as our Drug Development Fellowship. Cancer care is provided in close partnership with superlative colleagues in radiation oncology, a full complement of cancer specialized surgeons, radiologists, pathologists and the comprehensive faculty of UT Health San Antonio across medical specialties. UT Health San Antonio MD Anderson Cancer Center has been an NCI Designated Cancer Center for over 20 years with a robust research portfolio, three NCI programs, and a fully supported clinical trial infrastructure with over 200 active trials. UT Health San Antonio MD Anderson Cancer Center is the home to the world-renowned Institute for Drug Development and founded and co-hosts the San Antonio Breast Cancer Symposium (SABCS™), the largest breast cancer research symposium in the world.

The UT Health San Antonio is an Equal Employment Opportunity/Affirmative Action employer and is committed to excellence through diversity among its faculty, staff and students including protected veterans and persons with disabilities. All faculty appointments designated as security sensitive positions.

Dynamic practice leadership, communication and interpersonal skills, and keen strategic vision are required. Reporting is to the Director of UT Health San Antonio MD Anderson Cancer Center and the Chair of the Department of Medicine of UT Health San Antonio. Additionally, as this role will steward hematology and medical oncology within the shared cancer service line with MD Anderson Cancer Center, a link with corresponding MD Anderson Network® leadership will exist. The Chief will be responsible for continuing to build and evolve the Division to serve the cancer care needs for the population of the future, expand Division research programs and clinical trial accrual, and maintain high quality graduate medical education.

Candidates must have a medical degree and academic experience (consistent with eligibility for full professor with tenure), as well as meaningful practice leadership experience. Board certification in Hematology and/or Medical Oncology and eligibility for medical licensure in the State of Texas are required. The ideal candidate will have a widely recognized national reputation in their field and the ability to foster a culture of collaboration, innovation, and accountability across the UT Health San Antonio enterprise, UT Health San Antonio MD Anderson Cancer Center, and our region. This is a wonderful opportunity for a visionary leader. UT Health San Antonio is a research-intensive academic health institution with its primary campuses located in San Antonio in the South Texas Medical Center and sits as a gateway to the picturesque Texas Hill Country. Growing its population significantly, San Antonio is a vibrant, dynamic and multicultural city with much to offer, including an attractive cost-of-living.

Meyer Consulting has been exclusively retained to conduct this search. Applications (including a letter of interest and current CV), nominations, and requests for additional information should be directed to UT Health San Antonio MD Anderson's search consultants, Ryan Hubbs and Mike Meyer, via email at rhubbs@meyerconsultinginc.com. Phone: 509.415.5209 (Hubbs).

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JOSÉ BASELGA RESIGNS AS PHYSICIAN-IN-CHIEF AT MEMORIAL SLOAN KETTERING

By Paul Goldberg and Matthew Bin Han Ong

José Baselga has resigned from his position as physician-in-chief and chief medical officer of Memorial Sloan Kettering Cancer Center less than a week after The New York Times and ProPublica reported that he had failed to disclose his conflicts of interest in scientific and medical journals and at professional meetings.

After the conflicts—involving millions of dollars—were enumerated in an article published Sept. 9, Baselga attempted a *mea culpa* strategy while MSK pointed out that disclosure rules are vague and inconsistent.

The Cancer Letter's analysis of documents that emerged during this imbroglio demonstrates that Baselga didn't apply standard rules for disclosure, apparently believing, for example, that, in papers dealing with basic and translational research, conflicts are not subject to disclosure. Similarly, he seemed to believe that no disclosure was needed in papers on compounds that are no longer viable.

Documents made public during this controversy but until now not analyzed publicly suggest that Baselga's interpretation of disclosure was so idiosyncratic that all 178 papers that list him as an author during his time at MSK could be tainted. He disclosed conflicts on 72 of those papers, but adequacy of disclosure may need to be examined. The remaining papers—where no disclosure was made—add up to 105.

A story about Baselga's interpretation of disclosure rules and his inconsistent application of what he believed requirements to be appears on page 8.

"I fear my continued role leading clinical care and research will become too much of a distraction to the hospital and its remarkable team of physicians, researchers and staff," Baselga wrote in a resignation letter he submitted to Craig Thompson, MSK president and CEO, on Sept. 13. "I take full responsibility for failing to make appropriate disclosures in scientific and medical journals and at professional meetings."

Pledging to continue to update his own disclosures, Baselga called for greater consistency in disclosure requirements. "It is my hope that this situation will inspire a doubling down on transparency in our field and at MSK, other research institutions, industry, publications, professional societies and other stakeholders continue to work together to standardize the disclosure process," he wrote.

Baselga's resignation became effective immediately. His letter of resignation is posted here.

Announcing Baselga's resignation, Thompson wrote:

Dear MSK Colleagues,

Earlier today I accepted the resignation of José Baselga, MD, PhD, as Physician in Chief. His letter of resignation is here, and I believe it speaks for itself. It is effective immediately.

Dr. Baselga has made numerous contributions to our organization, our patients, and the field of cancer treatment and research. We are grateful for his service.

Lisa DeAngelis MD, currently the Chair of Neurology, will become the acting Physician in Chief while a search for Dr. Baselga's successor is conducted. Dr. DeAngelis is a leader in the field of neuro-oncology and is held in high esteem by her colleagues throughout MSK. We are thankful for her willingness to take on this challenging role.

Questions about Dr. Baselga's disclosures and relationships with outside organizations have caused concern from the community, our staff, and most importantly our patients and family members. As you know, MSK has robust programs in place to manage how our staff should work with outside organizations and we are confident of strong compliance in this area. We will remain diligent. There will be continued discussion and review of these matters in the coming weeks.

Everyone at MSK is united around the commitment to deliver the highest quality care. Our first obligation is to our patients and their wellbeing throughout treatment. In this we have never wavered.

Regards,

Craig Thompson
President and CEO

Mea culpa proved insufficient

Some of the information in the Times-ProPublica story was readily available.

Payments to physicians can be looked up on a government-run database. Key in "Baselga"—or any other name—and compare the results with disclosures made to journals and professional societies.

Journal editors—or, for that matter, college interns—can play this game with ease, but as a rule refrain from doing so, leaving it to authors to be guided by the honor system and relying on institutions to monitor ethics of their faculty members.

The Open Payments database extends through the end of 2017 and is limited to payments by companies with FDA approved, marketed products used by Medicare. Payments from private companies with drugs in development, as well as payments made in 2018, do not appear in Open Payments. Patents held by authors are also subject to disclosure, but are not listed in Open Payments.

Disclosed conflicts of interest rarely lead to rejection of a paper, while failure to disclose causes embarrassment and worse. Indeed, there is little doubt that had Baselga made appropriate disclosures to journals and professional societies, he would still have been able to publish and present. Many physicians and scientists have competing interests, but generally the rule of thumb is to err on the side of disclosing more rather than less.

When he was first contacted by reporters from the Times and ProPublica, Baselga attempted to explain his rationale for making disclosure, creating a document that instead revealed his misinterpretation of these rules and demonstrated the magnitude of the problem—and therefore his and MSK's potential exposure.

When the news story about Baselga's failure to disclose was published on Sept. 9, he attempted a mea-culpa-mea-culpa-*mea-culpa-mea-maxima-culpa* strategy, apparently hoping that this issue will be categorized as a problem of compliance with vague and inconsistent disclosure rules, and blow away.

The text of that email, which was obtained by The Cancer Letter, follows:

From: Baselga, Jose T./
Physician-in-Chief
Subject: message from
Jose Baselga

Dear MSK Colleagues,

I apologize if any of the coverage and comments in the New York Times and ProPublica has caused any of my colleagues at MSK any embarrassment or professional or personal discomfort.

I take responsibility for failing to make appropriate disclosures in scientific and medical journals and at professional meetings. I have already updated disclosures in medical journals and will continue to do so until the record is complete.

I want to be clear that while I may have been inconsistent in disclosing, the article does not question the validity of the research and the studies that were published.

I am committed to transparency and accountability in all of our dealings. That is my goal and I know I need to do better. I know you share my commitment to developing new treatments and medicines that will help our patients suffering from cancer.

I will be meeting with my team to discuss the article and will set up an opportunity to answer your questions and concerns. I value your inputs and trust.

Best regards,
Jose

It's not clear how widely the Baselga email was circulated prior to publication in The Cancer Letter.

According to the Times and ProPublica story, Baselga made "nearly $3.5 million in payments from drug, medical equipment and diagnostic companies from August 2013 through 2017," and that "since 2014, he has received more than $3 million from Roche in consulting fees and for his stake in a company it acquired."

According to the database, Genentech, a unit of Roche, paid Baselga a bit over $2.8 million for his stake in Seragon Pharmaceuticals Inc. A company press release identifies Baselga as a founding member of Seragon's clinical and scientific advisory board. Seragon was purchased for $725 million in cash. Subsequently, Genentech halted development of that company's lead product, a Selective Estrogen Receptor Degrader called GDC-0810.

In a Sept. 9 letter addressed to "MSK Colleagues," Thompson and Kathryn Martin, MSK chief operating officer, commented on the Times and ProPublica story, suggesting that the disclosure requirements are "nebulous" and that problem of insufficient disclosure may extend beyond Baselga.

"MSK and our faculty need to do a better job," they wrote. "In addition, we need to work with journal publishers and professional societies to standardize the reporting process," they wrote. "We have had ongoing discussions with the American Society for Clinical Oncology about their model, as well as the value of a common standard for oncology disclosures in journals and presentations."

Further, Thompson and Martin argued that issues of academic freedom are involved. "We also believe in supporting academic freedom and the ability of individual researchers to engage in the scientific process, including publication of results," Thompson and Martin wrote. "This extends to the judgment exercised by individual researchers and their responsibilities as authors with regard to disclosure."

The text of the Sept. 9 email from Thompson and Martin follows:

Subject: IMPORTANT MESSAGE FROM CRAIG THOMPSON AND KATHRYN MARTIN

Dear MSK Colleagues,

This morning's print edition of The New York Times carries a front-page story regarding an analysis of voluntary disclosures made by Dr. Jose Baselga to journals and at professional meetings. The matter of disclosure is serious.

MSK has robust programs in place to ensure the quality, safety and excellence of MSK's patient care and research. These programs govern how our staff should work with outside organizations, including the pharmaceutical industry. They apply to all members of the MSK community.

We have asked Dr. Baselga to review his disclosures and work with the various medical societies and journal editors to correct the record of appropriate papers and presentations as the journals and societies see fit. He started that process and has already been in communication with several organizations.

The issues surrounding author disclosures are complex, as there are nebulous guidelines about when and how to make voluntary disclosures. We also believe in supporting academic freedom and the ability of individual researchers to engage in the scientific process, including publication of results. This extends to the judgment exercised by individual researchers and their responsibilities as authors with regard to disclosure.

MSK and our faculty need to do a better job. In addition, we need to work with journal publishers and professional societies to standardize the reporting process. We have had ongoing discussions with the American Society for Clinical Oncology about their model, as well as the value of a common standard for oncology disclosures in journals and presentations.

We are supportive of ASCO's efforts in this area and the leadership demonstrated by that organization. The issue of disclosure extends well beyond the world of oncology and MSK will also look to the efforts of other organizations, including the Association of American Medical Colleges.

Our work with industry partners is integral to MSK's charitable mission of providing high quality cancer care, leading research, and medical education with the goal of improving cancer treatment. Collaboration with industry leaders, from early stage startups to large corporations, is necessary to focus on bringing better treatments to patients.

MSK will continue to promote transparency and accountability. And we encourage industry collaboration, as it is a driving force that has led to the approval of novel, life-saving cancer treatments for countless patients across the globe.

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A color-coded document Baselga created to explain himself instead illustrated the extent of his confusion and exposure

By Paul Goldberg

The discussions that took place in the executive offices of Memorial Sloan Kettering Cancer Center over the past week aren't publicly known. Ditto conversations at top-tier medical journals and professional societies, which are assessing the aftermath of José Baselga's systematic failure to disclose his conflicts of interest.

However, the extent of the disclosure problem created by Baselga, who stepped down as physician-in-chief and chief medical officer Sept. 13, can be assessed publicly—even in the comfort of one's own office—thanks to a document Baselga himself created in order to explain his rationale for disclosing some competing interests while remaining mum on others.

If the document he created in response to questions from reporters from The New York Times and ProPublica is an indication, Baselga was guided by a highly unconventional interpretation of disclosure requirements and was inconsistent in applying even his own version of these standards.

As a result, all of Baselga's 178 papers published between 2013 and now—while he was at MSK—may be tainted, experts say. Even in papers where Baselga has made a disclosure, the disclosure could be incomplete. Three other categories of papers, where he didn't disclose, are: papers where he believed no disclosure was required, papers where the need for disclosure was, in his view, debatable, and papers where he admits an oops. According to Baselga's analysis, 105 papers fall into these three categories.

Presentations made at meetings of professional societies are open to challenge, too.

Realizing that just one failure to disclose can ruin a career, most researchers consider it a safe practice to disclose everything, avoiding making their own judgments on relevance.

To explain his rationale to the Times and ProPublica, Baselga put together a list of the publications that cited him as an author between 2013 and 2018 and color-coded it, thus dividing his 178 publications into four categories:

- "Publications where I disclosed
- "Publications that represented basic laboratory or translational work
- "Publications where disclosures are debatable. Most of them concerned exploratory biomarkers or reporting the results of early clinical trials with experimental agents for which a decision had been reached at the time of publication to not develop further. These publications had no clinical nor financial implications.
- "Publications to be disclosed."

A table below illustrates this breakdown:

	disclosed	basic/translational	debatable	to be disclosed
2013	25	8	5	1
2014	21	6	5	2
2015	9	7	3	1
2016	7	19	5	4
2017	5	18	6	9
2018	5	4	2	
	72	**62**	**26**	**17**

Baselga's color-coded document—which is central to understanding what happened at MSK—was previously published by the Times and ProPublica, but, until now, hasn't been analyzed publicly. The document is posted here.

The Cancer Letter asked three ethicists to review Baselga's document:

"Dr. Baselga's method of distinguishing which publications require disclosure is at least odd and appears to misunderstand the whole point of disclosure. Science develops incrementally, with each investigation building on the next. Scientists reading basic science reports or reports on biomarkers, which were not at this point targeted to be further developed, need to be alerted by disclosures to possible bias.

"Disclosures of financial ties can be helpful as one evaluates the report. No one is questioning the integrity of Dr. Baselga's research, but the simple act of remembering one's financial ties and disclosing them is a helpful step in keeping us all honest about our work."

Rebecca Pentz
Professor of research ethics at Emory University Winship Cancer Institute

"As best I can tell, he seems to think unless his research involves a positive clinical trial, he need not disclose. I think. But, that standard is not what is expected by journals! Nor, if my speculation is right, does it make much sense in managing conflicts of interest which can arise in all manner of studies—basic, translational, negative and clinical.

"I think we should all be disclosing as required, but it is not all clear to me what difference disclosure makes. You still see many arrangements that raise an eyebrow or sometimes induce a yawn. I don't think disclosure is the answer to managing conflicts of interest."

Arthur Caplan
The Drs. William F. and Virginia Connolly Mitty Professor of Bioethics at New York University Langone Health and the founding director of the Division of Medical Ethics

"I looked this over. It is interesting to say the least with regard to the degree of parsing of the justification for non-disclosure that the investigator has undertaken—presumably after the fact. I think the principles which govern the reasons for why we ask investigators to disclose their potential and relevant COI prevent investigators from doing this kind of parsing. As well, my understanding of journal policies would prevent investigators from making these kinds of distinctions. That is, investigators should simply disclose their relationships, and the journals then can either, in turn, disclose these relationships within any articles they decide to publish or decide whether and which disclosures are relevant on their own and have those disclosed in the articles.

"As well, the very nature of the accepted definition of what a conflict of interest is, i.e., what a third party could perceive as a conflict that could cloud an investigator's judgement, would prevent investigators from making these kinds of determinations of what's relevant and what does not need disclosure. In fact, as it is in this case, it just seems too easy after the fact to judge the lack of disclosure coming as a result of clouded judgment—especially if the remuneration in some of these instances is as large as reported."

Christopher Daugherty
Professor of medicine and chair of the University of Chicago Medicine Biological Sciences Division Institutional Review Board

> "It just seems too easy after the fact to judge the lack of disclosure coming as a result of clouded judgment—especially if the remuneration in some of these instances is as large as reported."
>
> *– Christopher Daugherty*

The view that papers about basic laboratory and translational research do not require disclosure of competing interests is inconsistent with standards of most journals and professional societies, experts say. The same applies to studies focused on what Baselga describes as "exploratory biomarkers or reporting the results of early clinical trials with experimental agents for which a decision had been reached at the time of publication to not develop further."

An explanation of the standards of the International Committee of Medical Journal Editors, which are used by many journals, reads:

"This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work.

"You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

"Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research.

"Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

"For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed.

"For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company."

The standards of disclosure are now being applied to Baselga's work retroactively.

"The American Association for Cancer Research has a longstanding track record of ensuring scientific integrity and ethics," said an AACR spokesperson. "To this end, we regularly evaluate our policies and practices and are currently reviewing our conflict of interest guidelines. After this evaluation is completed, we will make any necessary revisions or updates.

"We are in review of Dr. Baselga's documentation and will issue any necessary updates of the disclosures, as we have for other authors of articles in our scientific journals. This information will be visible to future readers of the journal articles in question."

Baselga is a co-editor of *Cancer Discovery*, an AACR journal, and a past president of the professional society.

The American Society of Clinical Oncology is investigating, too.

"ASCO takes its disclosure and conflict of interest policies very seriously," a spokesperson for the professional society said to The Cancer Letter. "Based on the specific concerns raised in the recent New York Times/ProPublica article, we have begun an internal review of Dr. Jose Baselga's recent disclosures for annual meeting presentations as well as journal publications.

"Once ASCO staff have completed the internal review, ASCO volunteer leaders will be responsible for determining next steps, according to our established policies for both continuing education activities and journals. Once final decisions have been reached, they will be communicated to Dr. Baselga."

Baselga is in communication with the New England Journal of Medicine, a spokeswoman for the journal said. "We've received updated forms from Dr. Baselga, and we have questions for him that must be answered for them to conform with our requirements. We await his answers," said Jennifer Zeis, manager of communications and media relations for NEJM Group.

JAMA Editor-in-Chief Howard Bauchner, said his journal is investigating. "*JAMA* is currently working with Dr. Baselga to clarify his conflict of interest statements in *JAMA* and the *JAMA Network Journals*," Bauchner said in a statement.

The Lancet is looking into it as well. "We are investigating these claims, and take issues regarding conflicts of interests very seriously," said Seil Collins, head of media and communications at *The Lancet journals*.

A spokesperson for *Nature Research* said its guidelines for authors are clear.

"*Nature Research* journals require authors to declare to the editors any competing financial and/or non-financial interests in relation to the work described that could be perceived by readers as inadvertently or deliberately influencing their presentation of the research," the spokesperson said.

"The corresponding author is responsible for submitting a competing interests statement on behalf of all authors of the paper. This policy is clearly stated in our guide to authors, which also includes examples of financial and non-financial competing interests: http://www.nature.com/authors/policies/competing.html.

"Authors are encouraged to consider funding and employment while engaged in the research, as well as personal financial interests, such as stocks and shares, with organizations that may gain or lose financially through the publication of that specific paper.

"We believe that primary responsibility for ensuring that researchers' conduct is appropriate lies with their employers, rather than with journal editors. However, should we become aware that the COI statement attached to a published paper is not compliant with our policies, we will look into the matter carefully and will update the literature when appropriate to ensure that the scientific record is accurate."

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ASCO urges CMS to drop proposal that threatens to reduce access for Medicare cancer patients

Through a combination of payment reductions, some provisions of the 2019 Medicare Physician Fee Schedule proposed rule will undermine access to cancer care for Medicare beneficiaries, the American Society of Clinical Oncology wrote in a comment letter to the Centers for Medicare & Medicaid Services.

"For long-term success, Medicare must change course and develop payment policies to support rather than weaken the provision of cancer care in the United States," ASCO President Monica Bertagnolli wrote in the letter to CMS. "We urge CMS to refrain from finalizing any proposals that would result in any cuts in payments for cancer services and to work collaboratively with ASCO to implement global payment reforms, including the development and implementation of new APMs (Alternative Payment Models) that are widely available to all cancer professionals."

The ASCO comment letter makes the following points:

1. **2019 Medicare Physician Fee Schedule**

   - ASCO supports the proposal to reduce documentation burdens for Evaluation and Management services, but urges CMS not to pair it with reductions in payment that will negatively impact patient access to care. Reducing administrative burdens should not come at the expense of resources dedicated to cancer care.
   - ASCO urges CMS to withdraw the proposal to consolidate E&M payments and to create add-on codes for inherent visit complexity because it will reduce the resources that Medicare dedicates to its most complex patient populations—including patients with cancer.
   - ASCO opposes any changes to the indirect practice expense methodology to accommodate the flawed E&M payment policies because they would create unsustainable reductions in payment for drug administration and other services routinely delivered in cancer care.
   - ASCO appreciates that the agency does not intend to apply the proposed Multiple Procedure Payment Reduction (MPPR) to drug administration services and opposes any potential expansion of the MPPR that could apply to drug administration services delivered on the same date of service as an E&M visit.
   - ASCO urges CMS not to finalize the proposed reduction in the add-on rate for Part B drugs subject to payment through the Wholesale Acquisition Cost (WAC) methodology, but to instead focus on pursuing comprehensive solutions that drive value-based cancer care.

- ASCO supports expanding coverage and reimbursement for services that do not require face-to-face interactions, and urges CMS to finalize its proposal to pay for Virtual Check-Ins, Remote Evaluation of Pre-Recorded Patient Information, and Interprofessional Internet Consultations.

2. Additional Changes in Part B Payment Policy

- ASCO urges CMS to continue implementation of the appropriate use program for diagnostic imaging in an incremental manner. ASCO supports gradual expansion of the Appropriate Use Criteria program, including an educational and operational testing period in 2020.

3. 2019 Quality Payment Program

- ASCO appreciates the agency's prompt implementation of the exclusion of Part B drug payments from the Merit-Based Incentive Payment System payment adjustment and the eligibility calculation for the low-volume threshold.
- ASCO urges CMS to exclude all drug costs from the assessment of cost performance and refrain from increasing the weight of the cost performance category in the MIPS scoring methodology until the agency implements a cost measurement methodology that fairly and accurately assesses resource use in cancer care. ASCO urges CMS to prioritize developing episodes of care that are capable of fairly and accurately evaluating the cost of medical oncology services.
- ASCO encourages CMS to provide more complete feedback in response to improvement activity nominations to ensure nominating parties receive a clear justification of the agency's rationale for including or excluding nominated activities in the improvement activity inventory.
- ASCO commends CMS for reforming the Promoting Interoperability performance category measures to emphasize the exchange of health information.
- ASCO supports the removal of the Base Score and encourages the agency to complete its transition away from "all-or-nothing" scoring in the PI performance category by removing the requirement for MIPS participants to report data on each PI measure.
- ASCO encourages CMS to reconsider including the Verify Opioid Treatment Agreement measure as either a bonus or mandatory measure in the PI performance category and recommends the agency reassign this activity to the Practice Improvement category of MIPS.
- ASCO urges CMS to withdraw its proposal that would require Qualified Clinical Data Registries to enter a licensing agreement with CMS as a condition for approving QCDR quality measures.
- ASCO urges CMS to standardize the timeline for removing topped-out QCDR measures and MIPS measures to reporting in the MIPS Quality Reporting category.
- ASCO urges CMS to adopt the Patient Centered Oncology Payment Model as an Advanced Alternative Payment Model to promote ongoing patient access to cancer care and foster new value-based approaches to cancer care.
- ASCO supports the implementation of the Medicare Advantage Quality Improvement Demonstration Program to exclude professionals that participate in value-based arrangements with Medicare Advantage Organizations from MIPS reporting and the MIPS payment adjustments.

Advanced APMs in oncology

In ASCO's view, there is an urgent need to increase the number of Advanced APMs in oncology.

"The current Medicare fee-for-service policies are over-reliant on an outdated coding system that does not provide reimbursement to support services, that are essential for high-quality and high-value cancer care," Bertagnolli wrote in the letter. "These services include patient management, care-coordination and other supportive services that are necessary to optimize outcomes for cancer patients."

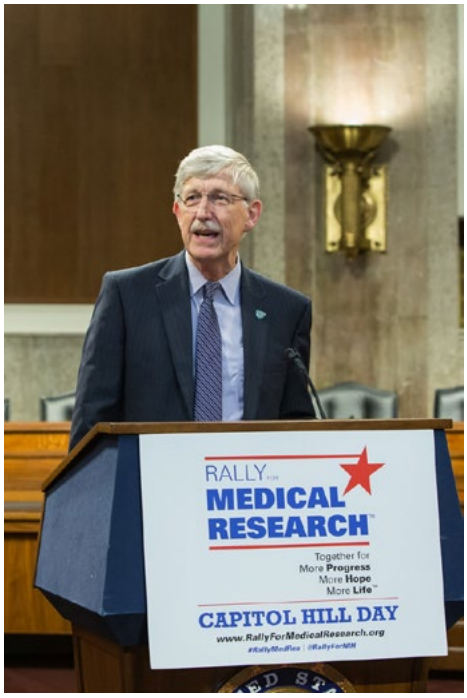
For example, ASCO said its PCOP model is designed to address challenges facing the cancer care delivery system today, since it adheres to value-based clinical pathways, and aligns physician reimbursement with the full range of services needed to treat patients with cancer.

Advanced APMs are needed in oncology to promote patient access to care and foster value-based approaches to treating cancer, ASCO said.

"ASCO urges CMS to expand and promote strategies that support oncology care, and in turn, some of the most complex—and costly—conditions Medicare beneficiaries face," ASCO leadership wrote in a statement. "Innovation that comes from designing alternative payment models would enhance both the quality and cost effectiveness of the care patients receive."

IN BRIEF

Nearly 350 groups join AACR in Rally for Medical Research



Nearly 350 organizations took part in the sixth annual Rally for Medical Research Hill Day—led by the American Association for Cancer Research—on Sept. 12 and 13 to advocate for sustained annual funding increases for NIH.

On Sept. 12, the reception included remarks from NIH Director Francis Collins, Sens. Roy Blunt (R-MO) and Patty Murray (D-WA), as well as Rep. Kevin Yoder (R-KS). Rep. Jamie Raskin (D-MD) spoke at breakfast on Sept. 13 to scientists, health professionals, and patient advocates who participated in the Rally for Medical Research Hill Day.

Advocates expressed their appreciation to Senate offices for passing a bill with a $2 billion funding increase for NIH in fiscal 2019, and requested that the House support the Senate-passed funding level of $39.1 billion for NIH in the latest version of the Labor-HHS appropriations bill.

"There is a very strong level of enthusiasm on Capitol Hill to provide the NIH with its fourth consecutive significant annual funding increase, which was underscored when the Senate voted overwhelmingly (85-7) last month for a bill that included a $2 billion increase for the NIH in FY 2019," Jon Retzlaff, chief policy officer of the AACR, said in a statement. "If the $2 billion increase proposed by the Senate is also supported by the House, it would translate to a 30 percent increase for the NIH since FY 2016."

The Rally for Medical Research was launched in April 2013.

Stand Up To Cancer 2018 telecast raises $123.6 million

Stand Up To Cancer said more than $123.6 million has been pledged collectively so far in connection with the Sept. 7 "roadblock" fundraising telecast in the United States and Canada.

The funds pledged toward the SU2C scientific model will be directed to collaborative research programs utilizing SU2C's scientific oversight in both the United States and Canada.

The live show was SU2C's sixth biennial fundraising telecast since the organization launched in 2008 and marks ten years of impact in the fight against cancer.

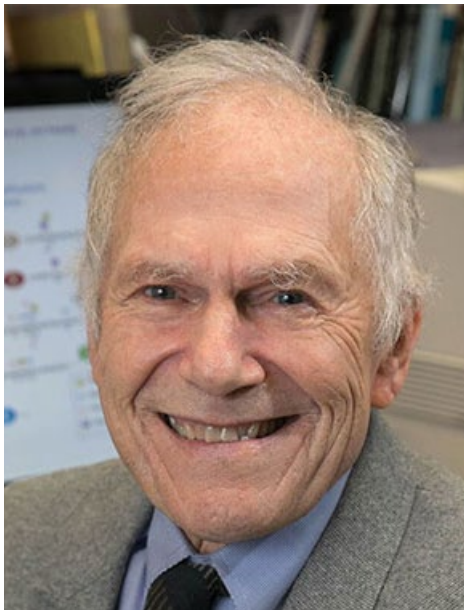
In the U.S., SU2C is still accepting donations at www.StandUpToCancer.org and at 1-888-90-STAND (78263).

The telecast is available at www.StandUpToCancer.org/show.

Allis, Grunstein, Glen, Steitz win 2018 Lasker Awards

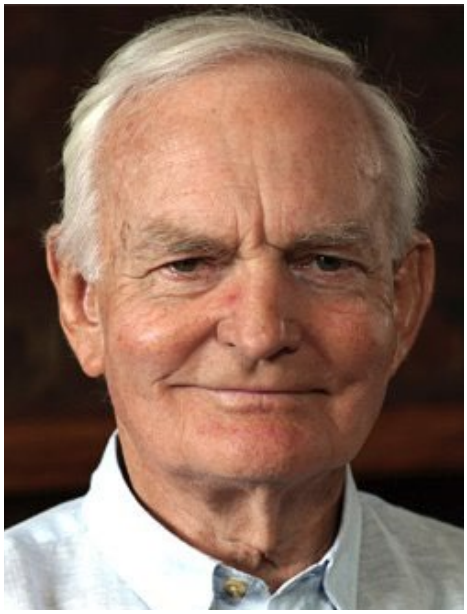
The Albert and Mary Lasker Foundation announced Sept. 11 the winners of its 2018 Lasker Awards:

C. David Allis



Michael Grunstien

C. David Allis from Rockefeller University and **Michael Grunstein** from the University of California, Los Angeles will receive the Albert Lasker Basic Medical Research Award, for discoveries elucidating how gene expression is influenced by chemical modification of histones—the proteins that package DNA within chromosomes.



John B. Glen, formerly from AstraZeneca, will be honored with the Lasker~DeBakey Clinical Medical Research Award, for the discovery and development of propofol, a chemical whose rapid action and freedom from residual effects have made it the most widely used agent for induction of anesthesia in patients throughout the world.

Joan Argetsinger Steitz from Yale University will receive the Lasker~Koshland Special Achievement Award in Medical Science, for four decades of leadership in biomedical science—exemplified by pioneering discoveries in RNA biology, generous mentorship of budding scientists, and vigorous and passionate support of women in science.

Widely regarded as America's top biomedical research prize, the Lasker Awards carry an honorarium of $250,000 for each category. The awards will be presented Friday, Sept. 21, in New York City.

$3.2 million NIH grant aims to correct diagnostic errors for breast cancer

In a new UCLA-led study, funded by a $3.2 million NCI grant, researchers will examine how perception and cognition interact in the interpretation of breast biopsy images. The aim is to improve physicians' diagnostic skills and accuracy.

Joann Elmore, a UCLA Jonsson Comprehensive Cancer Center member and professor of medicine in the David Geffen School of Medicine at UCLA, is leading the five-year project which will study diagnostic errors made by residents in training as well as experienced pathologists.

"Pathologists want to be better at their job and find every suspicious lesion, but when they do make errors, it can be hard to know why," said Elmore, who is also director of the UCLA National Clinician Scholars Program. "This project will use advanced eye-tracking techniques that measure exactly where the pathologist was looking during each case so that we can determine what is leading to diagnostic errors."

Elmore's previous research has identified high levels of disagreement and errors among physicians in the diagnosis of cancer.

CPRIT surpasses $2 billion milestone with 64 new grants

With the approval of 64 new research, product development, and prevention grants totaling more than $177 million, the Cancer Prevention & Research Institute of Texas has awarded $2.15 billion of the $3 billion approved by Texas voters in 2007 to fight cancer.

CPRIT's Academic Research program awarded 51 new grants to 16 different Texas institutions, including a Core Facility Support Award to Texas Southern University, a first-time CPRIT grantee. The awards are posted here.

CPRIT has awarded 1,317 grants totaling more than $2.15 billion. During the 85th Texas Legislature, CPRIT's Sunset Review date was extended by two years to 2023 to allow the agency to use fully all funds approved by Texas voters.

Sidney Kimmel – Jefferson joins Driver network

The Sidney Kimmel Cancer Center – Jefferson Health announced a collaboration with Driver, a first-of-its-kind global technology platform that connects cancer patients to the best treatments, which has launched in the United States and China.

Driver's platform enables any patient, anywhere in the world, to access treatment options across an unprecedented network of cancer centers without leaving home.

NCI and the Chinese National Cancer Center are the founding members of Driver's global network. To date, more than thirty leading cancer centers in addition to SKCC comprise Driver's network, including the Cleveland Clinic; Mayo Clinic; Massachusetts General Hospital; University of California, San Francisco; University of California, Los Angeles; Duke University; University of North Carolina; and Emory.

In order to provide patients with extensive cancer treatment options and information, Driver processes medical records and tumor data, then offers current evidence-based treatment guidelines as well as information on clinical trials for which a patient is potentially eligible that are being offered at any of the cancer centers in Driver's network.

Driver's lead investor is Horizons Ventures, with whom Driver has partnered from its inception to build its platform in China in parallel to the United States.

Three community health care systems to use Flatiron's OncoCloud Suite

Tennessee Oncology, New York Cancer & Blood Specialists, and West Cancer Center has joined up to form OneOncology, a technology platform that utilizes Flatiron Health's OncoCloud Suite, which includes OncoEMR, the company's electronic medical records management system.

OneOncology connects over 225 oncology providers who treat nearly 158,000 cancer patients every year at more than 60 care locations, according to the health systems. General Atlantic, a global growth equity firm, invested in OneOncology to ensure its "transformation to a value-based cancer care system."

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FUNDING OPPORTUNITIES

NCCN-Lilly RFP on quality of care in gastric cancer

The National Comprehensive Cancer Network announced a collaboration with Eli Lilly and Co. to offer a new opportunity seeking proposals to bridge gaps in care for gastric and gastroesophageal junction cancer patients in the U.S. The Request for Proposals outlines the scope and process that will be followed for the submission of Letters of Intent.

The intent of the RFP is to encourage U.S. organizations to submit LOIs describing concepts and ideas for developing, implementing, and evaluating programs that close clinical practice gaps and improve the quality of care for patients with gastric/GEJ cancer through adherence to evidence-based medicine guidelines, and improved competence and performance of health care providers and health care systems.

NCCN views this collaboration with Lilly as clear recognition of the advantages offered to industry and organizations treating cancer patients through the NCCN Oncology Research Program.

LOIs are due by 11:59 PM EDT, Wednesday, Oct. 24. Please direct questions in writing to Nicole Kamienski at kamienski@nccn.org with the subject line, "2018 Gastric Project."

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

Study details incidence and timing of immunotherapy-related fatalities

Vanderbilt-Ingram Cancer Center researchers have answered questions about the incidence and timing of rare but sometimes fatal reactions to the most widely prescribed class of immunotherapies.

Their research, which appeared in *JAMA Oncology*, is the largest evaluation of fatal immune checkpoint inhibitor toxicities published to date. They determined that although these severe events can happen, the risks are "within or well below" fatality rates for more common cancer treatments, including chemotherapy, stem cell transplants, and complex cancer surgeries.

The study was supported by NIH, NCI, The Cancer ITMO of the French National Alliance for Life and Health Sciences, the James C. Bradford Jr. Melanoma Fund and the Melanoma Research Foundation.

When fatal reactions did occur, they tended to happen early after starting treatment, on average 15-40 days, depending upon the type of immune checkpoint inhibitor. Their study further characterized the fatal toxicities and timing of reaction by type of cancer and specific drug.

"These drugs are quite transformative," said Douglas Johnson, senior author of the article. "The benefits outweigh the risks, but patients and doctors should be aware of their toxicities. These side effects can be quite severe, and they are something that we really need to pay attention to."

The team sorted through more than 16 million adverse drug reaction reports in a World Health Organization database searching for those related to immune checkpoint inhibitors. They also reviewed the records from seven academic centers, including Vanderbilt, that have been at the forefront of immunotherapy research. Additionally, they conducted a meta-analysis of published trials for the drugs.

Checkpoint inhibitors unleash the immune system to attack cancer, but they may also spur an attack on organs, including the heart, lungs, liver and colon. Steroids are prescribed to relieve myocarditis, pneumonitis, hepatitis, and colitis, and are usually extremely effective. Timely treatment with steroids is crucial, Johnson said.

"Some of the patients who died had a long delay before they received steroids," Johnson said. "In some cases, the patient didn't call in to report their symptoms or experienced a very unusual presentation that was difficult to diagnose."

The data also showed that older patients were more prone to experience fatal toxicities, although the occurrence was still rare.

"We don't necessarily think that older patients have more side effects, but when they do have toxicities, they can potentially have more complications," Johnson said.

The team found 613 fatal immune checkpoint inhibitor toxicities within the more than 16 million reports in the WHO pharmacovigilance database (Vigilyze) from 2009 to 2018.

Myocarditis had the highest fatality rate, as nearly 40 percent of patients with this side effect died.

The review of records from the seven academic centers revealed a 0.6 percent fatality rate. The meta-analysis of data from 112 clinical trials showed a fatality death rate ranging from 0.36 percent to 1.23 percent, depending upon the specific type of immune checkpoint inhibitor.

The study notes that this range is "dramatically lower than the near 100 percent fatality rate for metastatic solid tumors." The FDA has at this point in time approved immune checkpoint inhibitors for 13 different types of metastatic cancers.

"We have clinics full of patients now who received these treatments who are alive today because they responded to these treatments," Johnson said.

CARsgen Therapeutics and CrownBio complete CAR-T study for gastric cancer

Crown Bioscience has completed a joint study with CARsgen Therapeutics and Shanghai Cancer Institute, demonstrating the elimination of gastric tumors in mice using CLDN18.2 targeting CAR-T cells. The work was recently published in the *Journal of the National Cancer Institute*.

CAR-T cells were engineered to target Claudin18.2 and tested in gastric adenocarcinoma PDX models expressing high levels of Claudin 18.2.

"Humanized antibodies were developed and tested for their ability to redirect CAR-T cells on our PDX models. Tumor elimination was observed with no deleterious effect on normal gastric tissue in the mice, further validating it as high value CAR-T target and demonstrating a promising result for gastric and other CLDN18.2 positive tumors," said Henry Li, a co-author on the paper and senior vice president of research and innovation at Crown Bioscience.

Bavencio + Inlyta improved PFS in advanced RCC

Merck KGaA and Pfizer Inc. announced positive top-line results from the pivotal phase III JAVELIN Renal 101 study evaluating Bavencio (avelumab) in combination with Inlyta (axitinib), compared with Sutent (sunitinib) as initial therapy for patients with advanced renal cell carcinoma.

As part of a planned interim analysis, an independent Data Monitoring Committee confirmed that the trial showed a statistically significant improvement in progression-free survival by central review for patients treated with the combination whose tumors had programmed death ligand-1 positive expression greater than 1 percent (the primary objective), as well as in the entire study population regardless of PD-L1 tumor expression (the secondary objective).

According to the statistical analysis plan, if PFS was statistically significant in the PD-L1+ subgroup, then PFS in the entire study population was to be analyzed for statistical significance. JAVELIN Renal 101 will continue as planned to the final analysis for the other primary endpoint of overall survival.

No new safety signals were observed, and adverse events for Bavencio, Inlyta, and Sutent in this trial were consistent with the known safety profiles for all three medicines. The alliance intends to pursue a regulatory submission in the U.S. based on these interim results, and these results will be discussed with global health authorities. A detailed analysis will also be submitted for presentation at an upcoming medical congress.

In Dec. 2017, the FDA granted Breakthrough Therapy Designation for Bavencio in combination with Inlyta for treatment-naïve patients with advanced RCC. Despite available therapies, the outlook for patients with advanced RCC remains poor. About 20 to 30 percent of patients are first diagnosed at the metastatic stage. The five-year survival rate for patients with metastatic RCC is approximately 12 percent.

JAVELIN Renal 101 is a global Phase III, multicenter, randomized (1:1) study investigating the efficacy and safety of Bavencio in combination with Inlyta as a first-line treatment option compared with SUTENT monotherapy in 886 patients with advanced RCC across all risk groups.

The primary objectives are to demonstrate that Bavencio in combination with Inlyta is superior to Sutent monotherapy in prolonging PFS or OS in patients with PD-L1+ tumors. Bavencio was administered at 10 mg/kg IV every two weeks in combination with Inlyta at 5 mg orally twice daily; Sutent was administered at 50 mg orally once daily, four weeks on/two weeks off.

The combination of Bavencio and Inlyta is under clinical investigation for advanced RCC, and there is no guarantee this combination will be approved for advanced RCC by any health authority worldwide.

In the US, INLYTA is approved as monotherapy for the treatment of advanced RCC after failure of one prior systemic therapy. Inlyta is also approved by the European Medicines Agency for use in the EU in adult patients with advanced RCC after failure of prior treatment with Sutent or a cytokine.

IMV Inc. and Merck to evaluate DPX-Survivac + Keytruda

IMV Inc. said it has expanded its clinical program with a phase II basket trial evaluating its lead candidate, DPX-Survivac, in combination with low dose cyclophosphamide and Merck's anti-PD-1 therapy, Keytruda (pembrolizumab) in patients with select advanced or recurrent solid tumors.

"The clinical data from our recent ASCO meeting presentation demonstrated for the first time the unique potential of DPX-Survivac to generate solid tumor regressions in ovarian cancer," said Frederic Ors, chief executive officer of IMV Inc.

The open-label, multicenter, phase II basket study will evaluate the safety and efficacy of the immunotherapeutic combination agents in patients with bladder, liver (hepatocellular carcinoma), ovarian, or non-small cell lung cancers as well as tumors shown to be positive for the microsatellite instability high biomarker.

Investigators plan to enroll more than 200 patients across five indications at multiple medical centers in Canada and the United States. IMV expects to initiate trial enrollment in the 4th quarter of 2018.

This is the third clinical trial evaluating the combination of DPX-Survivac, low dose cyclophosphamide, and pembrolizumab in advanced recurrent cancers. Two ongoing investigator-sponsored phase II trials are evaluating this combination in patients with advanced ovarian cancer and diffuse large B-cell lymphoma.

DPX-Survivac is the lead candidate in IMV's new class of immunotherapies that programs targeted T cells in vivo. It has demonstrated the potential for industry-leading targeted, persistent, and durable T cell activation against cancer.

This mechanism of action is key to generating durable regressions in solid tumors, IMV said. DPX-Survivac consists of survivin-based peptide antigens formulated in IMV's proprietary DPX drug delivery platform. DPX-Survivac is believed to work by eliciting a prolonged cytotoxic T cell attack on cancer cells presenting survivin peptides.

Survivin, recognized by NCI as a tumor-associated antigen, is broadly over-expressed in most cancer types, and plays an essential role in antagonizing cell death, supporting tumor-associated angiogenesis, and promoting resistance to anti-cancer therapies. IMV has identified over 15 cancer indications in which the over-expression of survivin can be targeted by DPX-Survivac.

DPX-Survivac has received Fast Track designation from FDA as maintenance therapy in advanced ovarian cancer, as well as orphan drug designation status from the U.S. FDA and the European Medicines Agency in the ovarian cancer indication. It is currently being evaluated in multiple phase Ib/II clinical trials.

Clinical trial shows best outcomes to date for older Hodgkin lymphoma patients

Recently published results of a phase II clinical trial have shown the best outcomes to date for newly diagnosed older Hodgkin lymphoma patients treated with brentuximab vedotin given before and after doxorubicin, vinblastine and dacarbazine (AVD) chemotherapy, which is the standard of care.

Causes of poor outcomes for older Hodgkin lymphoma patients are not well understood although inability to tolerate full doses of chemotherapy, the existence of co-morbidities, disease biology, and other factors have often been attributed.

The aim of this multicenter, investigator-initiated study was to improve outcomes for this difficult to treat population. Results of the work were published in the September 4 online edition of the *Journal of Clinical Oncology* (doi: 10.1200/JCO.2018.79.0139).

In this study, participants who were initially untreated for their disease received two 'lead-in' doses of single-agent brentuximab vedotin, which were followed by six cycles of standard AVD chemotherapy. Responding subsequently patients received four brentuximab vedotin consolidation cycles. Enrolled were 48 patients with a median age of 69; 82 percent had advanced stage disease and 60 percent had high-grade co-morbidities.

The overall response rate to the initial brentuximab vedotin lead-in dose was 82 percent with a complete remission rate of 36 percent. After first-line chemotherapy was administered, the overall response rate and remission rates were 95 percent and 90 percent, respectively.

Additionally, the two-year progression-free survival rate was 84 percent with an associated overall survival rate of 93 percent on intent-to-treat analyses. In addition, baseline assessment of geriatric measures including activities of daily living and presence of co-morbidities was strongly prognostic for patient outcome in this study.

The authors said study limitations include the inability of some patients to complete therapy as planned (23 percent did not receive the prescribed six AVD cycles; 48 percent did not complete brentuximab vedotin consolidation cycles). Strategies to decrease the length of the therapy, either through individual drugs or number of cycles administered, should also be explored.

The research was funded as an investigator-initiated clinical trial via Seattle Genetics. An earlier version of the work was presented at the December 2017 American Society of Hematology Annual Meeting; and in part at the 10th International Symposium on Hodgkin Lymphoma in October 2016 in Cologne, Germany. Additional details including information on conflicts of interest can be found at: doi: 10.1200/JCO.2018.79.0139.

Children who develop ALL may have dysregulated immune function at birth

A study has found that neonatal concentrations of eight detectable inflammatory markers were significantly different in children later diagnosed with B-cell precursor acute lymphoblastic leukemia compared with controls.

The study, published in *Cancer Research*, a journal of the American Association for Cancer Research, was conducted by Signe Holst Søegaard, a fellow in the Department of Epidemiology Research at Statens Serum Institut in Copenhagen, Denmark.

"Our findings suggest that children who develop ALL are immunologically disparate already at birth," said Søegaard. "This may link to other observations suggesting that children who develop ALL respond differently to infections in early childhood, potentially promoting subsequent genetic events required for transformation to ALL, or speculations that they are unable to eliminate preleukemic cells.

Prior research indicates that ALL could develop in children because of an overreaction to infections in childhood, Søegaard said. This may hold promise for the prevention of childhood ALL through early immune modulation.

Søegaard and colleagues used data from Denmark's Neonatal Screening Biobank and nationwide registers to assess baseline characteristics of the immune system of children born in Denmark from 1995 to 2008, who at ages 1–9 years were diagnosed with B-cell precursor ALL, the most common ALL subtype in children.

They measured the concentrations of inflammatory markers, including cytokines and acute inflammatory proteins, on neonatal dried blood spots from 178 childhood ALL patients and 178 matched leukemia-free controls.

Inflammatory markers included interleukin-6, its soluble receptor sIL-6R, IL-8, IL-10, IL-12, IL-17, IL-18, transforming growth factor-1, monocyte chemotactic protein-1, and C-reactive protein.

"These markers were chosen to provide a broad picture of the neonatal immune response," Søegaard said.

The study found children who later developed B-cell precursor ALL had statistically significantly different neonatal concentrations of eight of the nine analyzed inflammatory markers, compared with controls. IL-10 concentrations were too low for accurate measurement.

Neonatal concentrations of sIL-6R, IL-8, TGF-1, MCP-1, and CRP were statistically significantly lower, while concentrations of IL-6, IL-17, and IL-18 were statistically significantly higher among B-cell precursor ALL patients, compared with controls.

"We also demonstrated that several previously shown ALL risk factors, namely birth order, gestational age, and sex were associated with the neonatal concentrations of inflammatory markers," Søegaard said. "These findings raise the interesting possibility that the effects of some known ALL risk factors partly act through prenatal programming of immune function."

Limitations of the study include the small number of studied inflammatory markers and the limited sample size, which made it impossible to detect potential differences in the association with inflammatory markers between subtypes of B-cell precursor ALL, Søegaard said.

"Importantly, our study does not inform about the nature of the associations observed, i.e., whether they are causal or consequential. Accordingly, further studies are needed both to confirm the findings and to identify the underlying mechanisms," she said.

The study was conducted in collaboration with researchers at Statens Serum Institut in Copenhagen, University Hospital Rigshospitalet, Copenhagen, and University of Southern California, Los Angeles. The research was sponsored by the Dagmar Marshall Foundation, the A.P. Møller Foundation, the Danish Childhood Cancer Foundation, the Arvid Nilsson Foundation, and the Danish Cancer Research Foundation. Søegaard declares no conflict of interest.

Drug for pancreatic cancer targets two genes at a time

A University of Houston researcher has developed a synthetic compound, MA242, that can inhibit two of the major pathways of highly aggressive pancreatic cancer.

Ruiwen Zhang, a Robert L. Boblitt Endowed Professor in Drug Discovery, has published his findings, along with research associate professor of pharmacology Wei Wang, in *Cancer Research Journal*.

The drug may be a first-in-class, new therapy for pancreatic cancer and a new conceptual framework for developing other drugs.

"We developed a synthetic compound that we call MA242, and it can deplete both proteins at the same time increasing specificity and efficiency of tumor killing," said Zhang. "In our molecular modeling study, MA242 is a potent dual inhibitor." Though man-made, the new compound is based on a type of sea sponge.

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Stromal depletion and immunotherapy also have been proposed to offer substantial promise for treating advanced pancreatic cancer, but their therapeutic impact remains unclear.

The two cancer-causing genes linked in pancreatic cancer are nuclear factor of activated T cells 1 and murine double minute 2, a gene that regulates, and depletes, the tumor suppressor gene called p53. If there is no tumor suppressor p53 present, MDM2 will cause cancer on its own. NFAT1 up-regulates MDM2 expression and encourages tumor growth.

Patients with pancreatic cancer have too much MDM2 and NFAT1, which has left these genes as open targets for cancer therapy. Numerous studies have shown reduced MDM2 can lead to decreased tumor growth and progression. Healthy individuals have low levels of MDM2 and NFAT1, but diet, nutrition and environment can cause higher levels in cells, said Zhang.

DRUGS & TARGETS

FDA approves moxetumomab pasudotox-tdfk for hairy cell leukemia

FDA has approved AstraZeneca's moxetumomab pasudotox-tdfk, a CD22-directed cytotoxin indicated for adult patients with relapsed or refractory hairy cell leukemia who received at least two prior systemic therapies, including treatment with a purine nucleoside analog.

The approval was based on Study 1053 (NCT01829711) in patients with histologically confirmed HCL or HCL variant requiring treatment based on presence of cytopenias or splenomegaly and who had received prior treatment with at least two systemic therapies, including one PNA. Eligible patients had serum creatinine ≤1.5 mg/dL or creatinine clearance ≥60 mL/min as estimated by the Cockcroft Gault equation. A total of 80 patients were enrolled; 77 with classic HCL and 3 with HCL variant. Patients received moxetumomab pasudotox-tdfk, 0.04 mg/kg as an intravenous infusion, over 30 minutes on days 1, 3, and 5 of each 28-day cycle for a maximum of 6 cycles or until documentation of complete response (CR), disease progression, or unacceptable toxicity.

Efficacy in HCL was evaluated by the blinded independent review committee-assessed rate of durable CR confirmed by maintenance of hematologic remission (hemoglobin ≥11 g/dL, neutrophils ≥1500/mm3, and platelets ≥100,000/mm3 without transfusions or growth factor for at least 4 weeks) more than 180 days after IRC-assessed CR. The IRC-assessed durable CR rate was 30 percent (24/80 patients; 95% CI: 20, 41). The IRC-assessed CR rate was 41 percent (33/80 patients; 95% CI 30,53).

The most common non-laboratory adverse reactions (≥20%) of any grade were infusion related reactions, edema, nausea, fatigue, headache, pyrexia, constipation, anemia, and diarrhea. The most common grade 3 or 4 adverse reactions (reported in at least ≥5% of patients) were hypertension, febrile neutropenia, and hemolytic uremic syndrome. Adverse reactions resulting in permanent discontinuation of moxetumomab pasudotox-tdfk occurred in 15 percent (12/80) of patients. The most common adverse reaction leading to discontinuation was HUS (5%). The most common adverse reactions resulting in dose delays, omissions, or interruptions was pyrexia (3.8%).

The recommended dose of moxetumomab pasudotox-tdfk is 0.04 mg/kg administered as a 30-minute intravenous infusion on days 1, 3, and 5 of each 28-day cycle for a maximum of 6 cycles or until occurrence of disease progression or unacceptable toxicity.

Boehringer Ingelheim acquires all ViraTherapeutics shares to develop next-gen viral-based therapies

Boehringer Ingelheim has acquired all shares of ViraTherapeutics, a biopharmaceutical company specializing in the development of oncolytic viral therapies.

ViraTherapeutics developed the lead candidate VSV-GP (Vesicular Stomatitis Virus with modified glycoprotein), which is being investigated alone and in combination with other therapies. The total transaction value of EUR 210 million is based on an option and share purchase agreement signed between the companies in Aug. 2016.

The lead investigational candidate leveraging the platform, VSV-GP, has shown promising results in pre-clinical models, especially in combination with key immune modulatory principles Boehringer Ingelheim is developing.

ViraTherapeutics was a portfolio company of the two venture investors EMBL Ventures and the Boehringer Ingelheim Venture Fund.