shining a light on PROGRESS

'Illumination & Innovation'

Highlights from the 2015 Annual Meeting of the American Society of Clinical Oncology®

May 29–June 2, McCormick Place, Chicago, IL

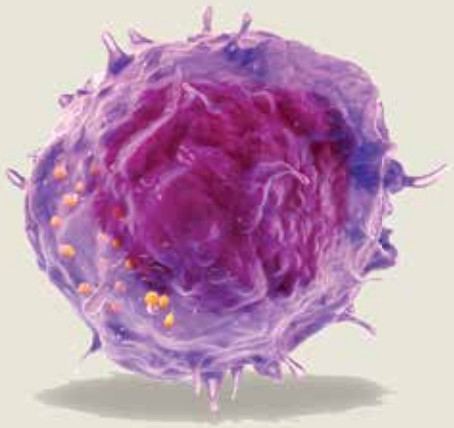
For AMCP Members and other Managed Care Professionals

AMCP Academy of Managed Care Pharmacy®

THERE'S A NATURAL KILLER INSIDE EVERYONE

WITH THE POTENTIAL TO TAKE ON MULTIPLE MYELOMA

Natural Killer Cells play an important role in the immune response to multiple myeloma.[1] However, disease burden increases as myeloma cells evolve to evade and suppress the body's natural immune response.[1-9]



Immuno-oncology is a fundamentally different modality under investigation for multiple myeloma and Bristol-Myers Squibb is researching the potential of the **SLAMF7, KIR,** and **CD137** pathways to activate the body's own Natural Killer Cells to target myeloma cells.

Rethink Multiple Myeloma

Bristol-Myers Squibb is deeply committed to furthering the science behind immuno-oncology by rethinking research and emphasizing the importance of a comprehensive approach to endpoint evaluation in multiple myeloma.

www.RethinkMultipleMyeloma.com

REFERENCES: 1. Jurisic V, Srdic T, Konjevic G, et al. Clinical stage-depending decrease of NK cell activity in multiple myeloma patients. *Med Oncol.* 2007;24:312-317; **2.** Bernal M, Garrido P, Jiménez P, et al. Changes in activatory and inhibitory natural killer (NK) receptors may induce progression to multiple myeloma: implications for tumor evasion of T and NK cells. *Human Immunol.* 2009;70:854-857; **3.** Jinushi M, Vanneman M, Munshi NC, et al. MHC class I chain-related protein A antibodies and shedding are associated with the progression of multiple myeloma. *Proc Natl Acad Sci USA.* 2008;105:1285-1290; **4.** Carbone E, Neri P, Mesuraca M, et al. HLA class I, NKG2D, and natural cytotoxicity receptors regulate multiple myeloma cell recognition by natural killer cells. *Blood.* 2005;105:251-258; **5.** von Lilienfeld-Toal M, Frank S, Leyendecker C, et al. Reduced immune effector cell NKG2D expression and increased levels of soluble NKG2D ligands in multiple myeloma may not be causally linked. *Cancer Immunol Immunother.* 2010;59:829-839; **6.** Cook G, Campbell JDM, Carr CE, et al. Transforming growth factor beta from multiple myeloma cells inhibits proliferation and IL-2 responsiveness in T lymphocytes. *J Leukoc Biol.* 1999;66:981-988; **7.** Yu J, Wei M, Becknell B, et al. Pro- and anti-inflammatory cytokine signaling: reciprocal antagonism regulates interferon-gamma production by human natural killer cells. *Immunity.* 2006;24:575-590; **8.** Nielsen H, Nielsen HJ, Tvede N, et al. Immune dysfunction in multiple myeloma. Reduced natural killer cell activity and increased levels of soluble interleukin-2 receptors. *APMIS.* 1991;99:340-346; **9.** Tinhofer I, Marschitz I, Henn T, et al. Expression of functional interleukin-15 receptor and autocrine production of interleukin-15 as mechanisms of tumor propagation in multiple myeloma. *Blood.* 2000;95:610-618.

Bristol-Myers Squibb

Immuno-Oncology

Engaging the World:
Knowledge into Learning

"We can't just be doctors. We have to engage the world. And the world is patients, healthy people, and the community." *–Peter Paul Yu, MD*

DR. PETER PAUL YU GIVES HIS PRESIDENTIAL ADDRESS.

For its 51st annual meeting, the American Society of Clinical Oncology® (ASCO®) received nearly 6,000 abstracts from leading scientists and medical professionals from around the world, presenting their research in the spirit of the conference's theme: "Illumination and Innovation: Transforming Data into Learning." The robust program, hosted in Chicago, IL, offered Extended Education sessions, panel discussions, poster presentations, and networking opportunities to further the conversation of how oncologists and researchers can use data to advance patient care and cancer treatment.

In his conference address to the press and ASCO® members, the organization's president, ***Peter Paul Yu, MD, FACP, FASCO,*** *said, "We arrive here with this great sense of excitement that everyone is here. The world is here. All our members are here... ASCO® is the premier scientific meeting venue for the cancer world." Dr. Yu noted that the conference boasts over 30,000 attendees—half of whom traveled to Chicago from outside of the United States, as a third of all members come from over 100 countries.*

Dr. Yu closed his remarks stressing the importance of reaching outside of the organization. "We can't just be doctors," he said. "We have to engage the world. And the world is patients, healthy people, and the community."

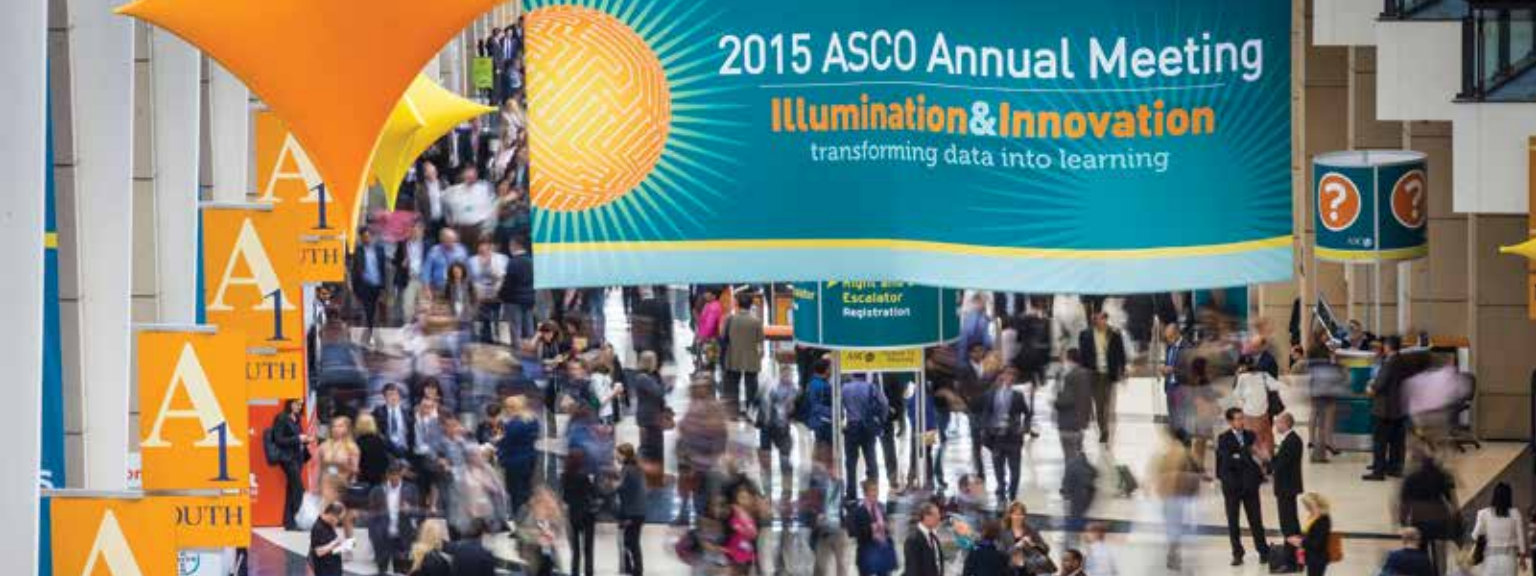
Information and Community:
A necessary partnership

In a letter to ASCO® members, ***Dr. Peter Paul Yu,*** *the organization's president, stressed that "cancer is not just about one patient and one doctor—it involves an entire community of caregivers working together on all aspects of the patient's treatment." He reinforced this sentiment in his conference address to press: "We know [conquering cancer] is not something we can do by ourselves. We need help from not only physicians, but also from patients, funders, and many others in—what is now called—the ecosystem."*

One growing aspect of the ecosystem is data—clinical results, electronic health records, meta-analyses, and even Twitter feeds. Dr. Yu wrote that "with data as a shared resource, we can accelerate learning from each other and from our patients, sharing new insights and making faster strides against cancer."

Is Online Patient Information at NCI Cancer Centers too Complex for Broad General Readership?

Online resources that are written too complexly, available on National Cancer Institute (NCI) Designated



Cancer websites, may be hindering their accessibility and impact on the public.

To foster wide readership comprehension, the National Institute of Health (NIH) and the Department of Health and Human Services recommend that online patient information (OPI) be written at a 6th grade reading level. Researchers from the Department of Human Oncology, University of Wisconsin, Madison, WI, questioned whether the level of readability of such websites met the literacy recommendations.

Researchers used *Cancer.gov* to isolate 68 NCI Designated Cancer Center websites, from which they then gathered both general OPI and specific OPI on colon, prostate, lung, and breast cancer. Drawing from 10 well-known readability tests—the New Dale–Chall Test, Flesh Reading Ease Score, Flesh-Kinkaid Grade Level, FORCAST test, Fry Score, Simple Measure of Gobbledygook, Gunning Frequency of Gobbledygook, New Fog Count, Raygor Readability Estimate, and Coleman-Liau Index—study authors evaluated the sites' OPI readability. As a secondary analysis, researchers compared the OPI literacy levels of comprehensive and non-comprehensive cancer centers, by geographic region, and to OPI that had been created specifically by the American Cancer Society(ACS).

Ultimately applying eight readability measurements to determine a grade level for each website, study authors revealed that 18 non-comprehensive and 40 comprehensive NIC Designated Cancer Centers exceeded literacy recommendations—the mean grade level of 12.46 (95% CI: 12.13 – 12.79) was significantly greater than the target reading level of 6th grade ($t(57) = 38.15$, $p < .001$). Information provided by the ACS was closest to the target readability, with OPI written at 7-9th grade reading levels. No difference in readability was evident between comprehensive and non-comprehensive centers.

The findings raise further questions regarding whether or not vital cancer information is reaching and impacting patients and the public.

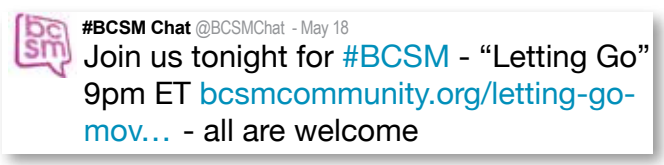
Rosenberg S, et al. Abstract #6526. June 1, 2015.

Disease-Specific Hashtags for Online Communication about Cancer Care

Cancer-specific hashtags used on Twitter have the potential to increase valuable interaction between stakeholders in cancer care.

Researchers at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, and Massachusetts General Hospital, Boston, MA, recognized the increased number of patients and health care professionals online. The authors posited that disease-specific cancer hashtags could not only increase productive interactions, but could also foster access to health information. Using #bcsm and #btsm, two de novo hashtags, study authors designed the cancer tag ontology (CTO) for online use.

Using data from Symplur, LLC, the retrospective study of 25 hashtags that appeared on Twitter from April 2011 to September 2014 allowed for researchers to categorize up to 100 active users of each of the following hashtags: patient; doctor; non-doctor health care professional (HCP); individual NOS (I); health care organization (HCO), other organization (OO); or spam.



#BCSM HASHTAG INVITES CONVERSATION FROM THE BREAST CANCER COMMUNITY.

The quarterly review of tweets revealed 531,765 tweets from 77,454 users of which 11% were patients, 20% doctors, 3% HCP, 32% I, 30% HCO, 1% OO, and 3% spam. The two original hashtags #bcsm and #btsm had the most use with 249,312 and 110,465 tweets, respectively. New tags, accounting for 93% of the analyzed activity, materialized from Twitter-based discussions and included: #ayacsm; #gyncsm; #lcsm; #mmsm; and #pancsm.

While it was clear to study authors that it is possible to grow organized, cancer-specific hashtags on Twitter, they stressed that further study will help determine if CTO could affect access, outcomes, or act as a model throughout the medical field.

Katz MS, et al. Abstract #6520. June 1, 2015.

Cancer Mortality and Published Research Output: Is There Any Relationship?

A new study from Canada suggests that the output of cancer research may positively impact cancer funding. With the growth of published cancer research, investigators sought to explore whether or not research output and clinical trials are proportional to study funding or mortality by cancer site.

Using the 2013 Statistics from the American and Canadian Cancer Societies, researchers established the 10 most prevalent causes of cancer death that year. The 2011 results from the Canadian Cancer Research Alliance offered the total amount of research funding. All 2013 journal articles (19,361) and clinical trials (2,661) published by U.S./Canadian authors for those cancer sites were gathered from the OVID MEDLINE database. Study authors used this information in conjunction with descriptive statistics and the Pearson correlation coefficient (r) to establish the relationship between research output of publications and clinical trials, cancer mortality, and research funding.

Research output for lung (41% deaths, 15% publications, 16% clinical trials), colorectal (14%, 7%, 6%), pancreas (10%, 7%, 5%), and gastroesophageal (7%, 5%, 3%) cancers were found to be substantially lower proportionally. Moreover, significant variations were seen in research funding across research sites: Total investment in 2013 in Canada per cancer death was $599 for bladder cancer, $1,039 for lung cancer, $2,197 for colorectal cancer, $9,212 for prostate cancer, and $14,329 for breast cancer.

While study authors found an association between the level of research output and research funding (all publications $r = 0.8942$ $p < 0.001$; clinical trials $r = 0.9258$, $p < 0.001$), a relationship between output did not show any significant correlation to cancer mortality.

Patafio F, et al. Abstract #6595. June 1, 2015.

Conflict of Interest (COI) Slides Not Displayed Long Enough

Conflict of Interest (COI) slides are shown to alert scientific audiences to possible financial biases presenters may have. Investigators questioned whether these slides were displayed long enough. Researchers reviewed the 2014 Annual Meeting of the American Society of Clinical Oncology® archived presentation videos, studying the disclosures and display time (DT) of the COI slides. They then created a predictive model that assumed that 1 second is required to focus on COI slides, with more time needed to understand multiple categories and relationships listed. Researchers found the COI slides were visible, on average, only 1/65 seconds, and concluded the DT for sound comprehension was not enough for audiences to fully grasp conflicts of interest that may be present.

Talcott JA, et al. Abstract #6576. June 1, 2015.

Value and the Cost of Care

The conference revealed ground-breaking and forward-thinking advances toward treating and curing cancer. But with many of the trial results and education sessions looking to the future, oncologists and other medical professionals were forced to reflect on barriers that prevent those advancements from becoming actualized. A systemic obstacle for oncologists and their patients is, of course, cost of care.

In a May 27 pre-conference interview conducted by Medscape, ASCO® president ***Dr. Peter Paul Yu*** *shared his own thoughts on the problem. Like many in his field, he questioned: "What good is it to have really great drugs if they're so expensive that people either go broke trying to get them or can't afford them and just can't get them? We're realizing more and more that with this bounty of new drugs at the prices they're coming out at, we really need to look carefully and say, 'It's a great drug but where is its niche? It's not that everybody needs to get this drug. Where does it really add value?'"*

Dr. Yu argued that the problem is far-reaching: "We're looking more and more at global oncology, at health care in low- and middle-income countries. Again, it's the extension of the idea that, 'It's great to have wonderful therapies, but if people can't afford it or there isn't the infrastructure to deliver it, then we really haven't done the job.'"

How Should Costs of Care Attributable to Cancer Be Estimated?

How total costs attributed to cancer are determined can significantly impact the proportion of total cost *attributed* to cancer, according to a new study presented by researchers from the Dana Farber Cancer Institute, Boston, MA, and the University of Colorado Cancer Center, Denver, CO.

Total cost of medical care is distinct from cost of care attributable to cancer. Study authors argue that transparent approaches are necessary to contextualize decisions about value of interventions. But how can these separate costs be determined? Researchers measured how different methods for specification of cancer-free control cohorts affected estimation of cancer-attributable costs.

To start, researchers calculated mean Medicare spending from one month prior until 11 months after diagnosis among patients > 66 diagnosed with lung, breast, prostate, and colorectal cancers from 2007-2009, using SEER-Medicare data. Cancer-attributable costs were then assessed by subtracting monthly expenditures for cancer patients from one of three reference cohorts: 1. non-cancer Medicare patients individually matched by age, gender, race, and SEER region; 2. non-cancer

TABLE 1: **Cancer-Attributable Costs, by Reference Group (% Total Costs Attributed to Cancer).**

	Total costs	Non-cancer patients, demographic match	Non-cancer patients, demographic and comorbidity match	Cancer patients as own control, year prior to diagnosis
Lung n = 43,196	47,366	31,703 (67)	28,725 (61)	35,476 (75)
Breast n = 33,674	30,958	14,653 (47)	15,242 (49)	22,749 (73)
Prostate n = 42,079	25,126	9,774 (39)	11,048 (44)	18,320 (73)
Colorectal n = 29,075	54,144	38,184 (71)	37,235 (69)	43,621 (81)

Chen AB, et al. Abstract #6503. May 30, 2015.

Medicare cohort matched on demographic factors with the addition of modified Charlson comorbidity score, 3) monthly costs from 2 to 13 months prior to diagnosis, using cancer patients as their own control.

Notably, when using non-cancer controls and matching by comorbidity in addition to demographic characteristics, the attributable costs were greatest in breast and prostate cancer patients, and less for lung and colorectal. Prostate cancer showed the greatest variation in reported cost of care: Non-cancer patients, demographic match mean cost was $9,774, while cancer patients used as their own control reported a mean cost of $18,320 for the same kind of cancer (see TABLE 1). Cancer-attributable costs were highest for all patients when calculating based on their own pre-diagnosis costs as comparison.

The study findings clearly show that the reference group used in calculating cost of care can significantly impact the costs attributed to cancer and should be clearly demarcated when determining cost and value.

Chen AB, et al. Abstract #6503. May 30, 2015.

Medication Adherence Affected By Cost in Cancer Survivors

Nonelderly long-time cancer survivors privilege saving money over following their prescription medication as needed, according to a new study.

Researchers from the American Cancer Society wanted to know if finances for nonelderly and elderly cancer survivors in the U.S. affected whether or not they followed their prescription medication. Using the National Health Interview Survey from 2011 to 2013, recently diagnosed and previously diagnosed cancer survivors, as well as respondents who had no cancer history, were identified.

Survey questions addressed medication compliance patterns and money-saving actions. Previously diagnosed cancer survivors were more likely to neglect prescription medication in order to save money compared to individuals without a cancer history, primarily among nonelderly cancer survivors (nonelderly: 18-64; elderly: 65+):

1) skipped medication doses (8.6% vs 6.7%);
2) took less medicine (9.3% vs 7.0%);
3) delayed filing a prescription (11.7% vs. 8.8%);
4) asked doctor for lower cost medication (22.5% vs 17.2%);
5) bought prescription drugs from another country (2.5% vs 1.9%); and
6) used alternative therapies (6.3% vs 5.0%).

All analyses were classified by age, and multivariable logistic regressions were fitted to approximate the adjusted percentage of individuals who reported non-compliance for prescription medication, controlling for age, sex, race/ethnicity, marital status, education, number of comorbidities, health insurance, and geographic region.

To compare, all recently diagnosed cancer survivors did not vary statistically from individuals without a cancer history when asked if financial reasons affected following prescription medication.

Jemel A, et al. Abstract #9590. May 30, 2015.

Cancer Patients and Their Willingness to Pay for Appointments

Cancer patients are not always willing to attend or pay for every health care appointment. Because a limited amount of comparative data exists on how cancer patients decide which appointments to attend, researchers from Australia used a discrete choice experiment (DCE) to gain further insight into patient preferences for their care and patients' perceived trade-offs between different appointment factors.

Individuals diagnosed with cancer at three hospitals were enlisted to complete a self-administered DCE. The questionnaire addressed six characteristics, which were evaluated using logistic regression, and willingness to pay (WTP) was derived from estimates of the different factors:

- Expertise of the doctor;
- Familiarity of the doctor with the patient's medical history;
- Waiting time for an appointment;
- Permitted accompaniment by family/friends;
- Travel times to appointments; and
- Out-of-pockets costs.

About one third of the 512 patients returned the questionnaire (36%). Of these, the main demographics were women (60%) of a mean age of 61, with a mean diagnosis period of 34 months (61% in the early stages of the disease), 90% of them having received cancer treatment. The results showed that patients most valued the expert doctor who was familiar with the patient's history. The distance travelled affected WTP the least.

The monetary findings of what patients were willing to pay are as follows:

- $705 to consult a specialist with higher expertise;
- $572 to consult doctors familiar with their medical history;
- $464 for shorter waiting times for appointments;
- $410 to be accompanied by family/friends; and
- $342 for shorter travelling times to appointments.

"Our study could guide the development of patient-centered health care models, with an emphasis on the most important appointment characteristics; models should improve patient access to experienced doctors, and support the role of primary care providers in the community," said investigators. "Interventions to reduce waiting and travel times for appointments and to accommodate medical escorts still influenced patient choices, but to a lesser degree."

Wong SF, et al. Abstract #6527. June 1, 2015.

Financial Burden for Cancer Patients in Clinical Trials: Impact of an Equity Program Intervention

New study findings show that some cancer patients who participate in clinical trials (CT) face significant financial barriers. Researchers questioned the impact of cancer care equity program (CCEP) on clinical trial participation, and analyzed the low enrollment among underserved groups.

Study authors enacted a CCEP at Massachusetts General Hospital (MGH) in 2014 to help fund non-clinical expenses related to CTs (e.g. travel, lodging). After providing financial assistance to CT participants, enrollment in 2014 (after initiating the CCEP) to 2012 and 2013 were compared. Researchers also administered surveys to CCEP patients and a comparison group of non-CCEP patients. Multiple regression analysis to evaluate changes in CT enrollment were also used.

The results showed that, in 2014, cancer CT enrollment increased by 17% and 40% compared to 2012 and 2013; results were adjusted for CT availability, phase, and cancer type.

Enrollment increased for racial minorities, those who lived greater than 50 miles from MGH, and for women, showing that financial assistance can increase the representation of underserved groups in CTs.

CCEP patients self-reported in the study survey that they had financial concerns in medical costs, travel, lodging and insurance coverage; their financial worry was greater than that of non-CCEP participants.

[Clinical trial] patients self-reported in the study survey that they had financial concerns in medical costs, travel, lodging and insurance coverage.

The presenters stressed: "While CTs often represent the best option for patients with cancer, patients served by the CCEP report significant financial barriers to CT participation. These findings stress the need to recognize and address the financial burden of CT participation."

Nipp RD, et al. Abstract #6501. May 30, 2015.

SUZANNE ELEANOR DAHLBERG, PHD, PRESENTS BASKET TRIAL DESIGNS.

Overcoming Barriers to Innovation

The presenters worked throughout the weekend to fulfill this year's theme focus of "Innovation." To be sure, many of the sessions did offer late-breaking clinical trial results and other research that is—as ***Jonathan S. Berek, MD,*** *Co-Chair of ASCO®'s Management of Cervical Cancer Guideline Expert Panel stated—"truly practice changing."*

But in the midst of these shared innovations, many of the sessions focused on the sweeping and specific barriers that the medical community faces—issues that hinder innovation. These presentations, posters, and discussions meditated on the question, But how? How do we innovate? A cursory search of "how" in the conference directory revealed at least 20 multi-presentation sessions and 194 abstracts asking or answering this very question: How?

Dr. Berek, in a pre-conference letter published on ASCO®'s website, expressed that this question is of utmost importance for the conference: "How do we bring the value of new discoveries to our patients?"

How Can We Improve Clinical Trial Efficiency? Think Outside the Box

The Extended Education session "Improving Clinical Trial Efficiency: Thinking Outside the Box" discussed the adaptive enrichment design strategies that have developed over the last 2-3 years, representing fresh tactics to hasten drug development so that the correct therapies can be provided to the correct patients as quickly as possible.

In an accompanying educational article from the ASCO® *2015 Educational Book,* co-authored by the panel chair **Sumithra J. Mandrekar, PhD,** Mayo Clinic, published as a resource for conference participants, the authors reflected on the need for such innovation: "The traditional drug development paradigm of phase I for establishing the safety profile, followed by phase II for efficacy signal, followed by phase III for establishing definitive clinical benefit is challenged by the use of targeted therapeutics and incorporation of biomarker assessment

> The fundamental challenge for development of new cancer therapeutics is therefore to be able to identify and assess activity in molecularly defined patient subsets starting from early phase trials to predict which patients will respond to a new agent/regimen.

MOTHAFFAR F. RIMAWI, MD, SHARES RESEARCH ON ANTI-HER2 THERAPIES.

for medical treatment." Though this traditional method has yielded "notable success," the presenters commented that finding the right drug for the right tumor remains "rudimentary."

"The fundamental challenge for development of new cancer therapeutics is therefore to be able to identify and assess activity in molecularly defined patient subsets starting from early phase trials to predict which patients will respond to a new agent/regimen," they wrote.

Session presenters outlined the three primary approaches that evolved:

- "The **enrichment design**, also called targeted design. Patients are screened with the diagnostic test and those who are considered 'test-positive' are eligible for the clinical trial. Eligible patients are randomized to receive either the test drug or an appropriate control regimen."
- **"Umbrella trials** [that] incorporate a central infrastructure for screening and identification of patients with a focus on a single tumor type or histology; multiple subtrials that test targeted therapeutics within molecularly defined subsets are embedded within the umbrella framework."
- **"Basket trial designs** [that] offer the possibility to include multiple molecularly defined subpopulations, across histologic subtypes or tumor types, in one cohesive design to evaluate the targeted therapy in question."

The presenters noted the increasing popularity of these methods as researchers work to treat their patients as quickly and effectively as possible.

Simon R, Mandrekar SJ, Dahlberg SE. Education Session. May 31, 2015.

How Can We Overcome Drug Resistance in Targeted Therapy of Cancer?

An Extended Learning session offered three examples of barriers to curing cancer, despite the innovations made in the field: 1. Resistance to Anti-HER2 Therapies in Breast Cancer, presented by **Mothaffar F. Rimawi, MD;** 2. Resistance to Tyrosine Kinase Inhibitors in Lung Cancer, presented by **Christine Marie Lovly, MD, PhD;** and 3. Resistance to Targeted Therapies in Gastrointestinal Cancers, presented by **Josep Tabernero, MD, PhD.**

Take-aways from each presentation:

- *Resistance to Anti-HER2 Therapies in Breast Cancer:* "HER2 is amplified or overexpressed in 20% to 25% of breast cancers. HER2 is a redundant, robust, and powerful signaling pathway that represents an attractive therapeutic target. Anti-HER2 therapy in the clinic has resulted in significant improvements in patient outcomes." Resistance happens for a number of reasons: "pathway redundancy, reactivation, or the utilization of escape pathways."

  Dr. Rimawi noted: "Deciphering these resistance mechanisms is necessary to better tailor therapy to individual patient tumors, optimize patient outcomes, and avoid unnecessary toxicity and cost."

- *Overcoming Resistance to Anti-EGFR Therapy in Colorectal Cancer:* "EGFR is a validated target for cancer therapeutics, with cetuximab and panitumumab leading to significant overall survival benefits when added to first-line chemotherapy in patients with genomically selected (all RAS wild type) metastatic colorectal cancer." Several genetic alteration cause resistance to anti-EGFR monoclonal antibodies. Furthermore, "Resistance to anti-EGFR therapy in colorectal cancer is also related to nongenetic mechanisms, such as compensatory activation of parallel receptor tyrosine kinases and over-

expression of ligands involved in paracrine signaling networks in the tumor microenvironment."

Dr. Tabernero argued: "Knowledge of the specific genetic mechanisms of drug resistance and the compensatory parallel signaling activation that occurs during anti-EGFR exposure have been fundamental for the study of alternative kinase inhibitors... [and] because targeted gene analysis does not always explain the mechanism by which CRC becomes resistant to anti-EGFR therapy, we believe that additional research should be directed toward understanding and controlling the evolutionary process in tumors."

- *Combating Acquired Resistance to Tyrosine Kinase Inhibitors in Lung Cancer:* "Treatment for patients whose lung tumors harbor specific oncogenic mutations often results in dramatic response to targeted therapies, such as tyrosine kinase inhibitors (TKIs)... Resistance can be either primary (de novo) or acquired. Specifically, acquired resistance is defined by tumor growth after initial tumor regression... Mechanisms of acquired resistance include drug target gene modification (amplification, second-site mutations), activation of bypass tracks, which serve as compensatory signaling loops, and/or histologic transformation."

  Dr. Lovly stressed: "A thorough understanding of the mechanistic basis for acquired resistance and the development of innovative therapeutic strategies to overcome resistance are paramount to most effectively combat resistance and, therefore, to improve the care of patients who have lung cancer."

Rimawi MF, Lovly CM, Tabernero J. Education Session. May 31, 2015.

How Can We Improve Access to Cancer Care for Veterans with Lung Cancer?

Specialized projects with the goal of improving quality of cancer care can significantly improve cancer treatment for underserved groups—such as veterans, according to a new study. The study, "Improving veteran access to lung cancer care (IVaLuCancerCare): A quality improvement project at the Louis Stokes Cleveland VA Medical Center (LSVAMC)," sought to identify and improve three shortcomings of lung cancer care for veterans: timeliness of care, coordination of care, and access to palliative care.

Researchers, through a grant from the VA Office of Specialty Care Transformation, developed a multidisciplinary program to help the 190 new veterans diagnosed with lung cancer every year and the 450 veterans who are followed for lung cancer care.

Toward this end, study authors implemented the program, in conjunction with the VA Center for Applied Systems Engineering, consisting of dedicated weekly lung cancer clinics and patient navigators, weekly lung tumor boards and nodule rounds, new education clinics and tracking tools, screening and management, and other interventions.

The main goals were to increase the percentage of veterans receiving palliative care from 0% to 30%, to increase medical oncology visits of 2 or more additional consultations on the same day from 33% to 50%, and to increase the number of veterans with non-small cell lung cancer who receive their first treatment within 4 weeks of diagnosis from 33% to 50%.

Using the "IVALuCancerCare" project at the LSVAMC, these goals were met. "We plan to sustain and spread the above changes and identify new ways to further enhance our program," said study authors.

Malhotra S, et al. Abstract #9593. May 30, 2015.

How Can Precision Medicine Benefit Cancer Patients?

Precision medicine (PM) is a rising trend across the medical field. Since President Obama announced a PM initiative, both the U.S. House and Senate confirm that it is something to be taken seriously—from individual patients to national policy at the Federal level.

In one of the featured press briefings, "Innovations in Precision Medicine for the 21st Century," session moderator **Clifford A. Hudis, MD, FACP,** outlined the three challenges of PM in terms of oncology: 1. How to find new ways to test drugs according to molecular characteristics of tumors; 2. How to learn from every patient; and 3. How to harness data in powerful new ways.

The Targeted Agent and Profiling Utilization Registry (TAPUR) study was the main focus of the briefing. TAPUR recognized the findings of Van Allen et al. that a large proportion of cancers may contain at least one plausibly actionable genetic alteration, and that a conventional clinical trial design approach may not be possible to address the fact that individual patients may need more than sweeping trial result.

Often, patients with advanced cancer have no standard medication options. When genomic profiles are performed, actionable variants are sometimes detected. The issue, then, is how to get patients targeted drugs, and how to learn from the treatment to help other cancer patients.

To address this, TAPUR will seek to observe the practices of prescribing targeted therapies to individuals with advanced cancer whose tumor reveals a genomic agent know to have a target drug. The other primary objective is to facilitate patient access to available anti-cancer drugs that may have potential efficacy.

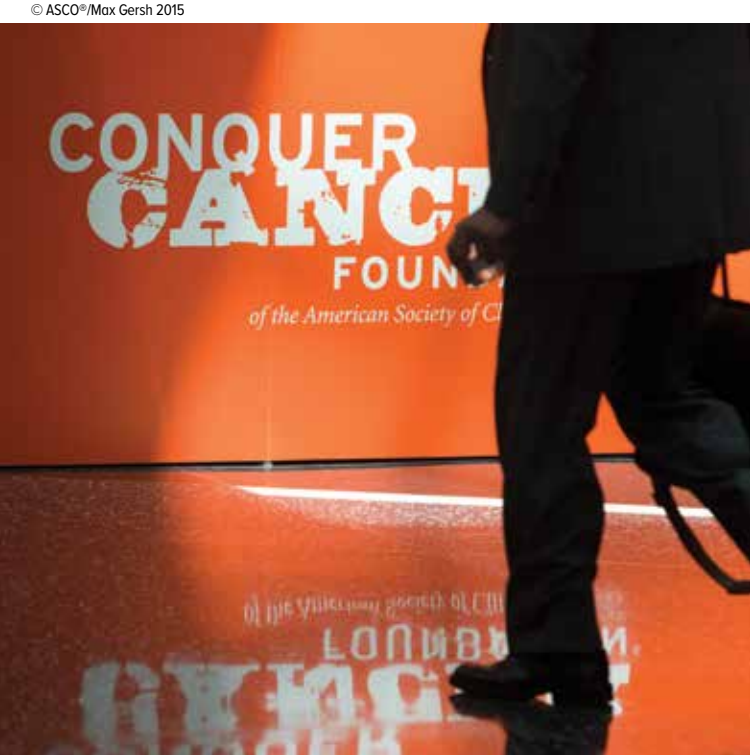
Study participants will be chosen on the following characteristics: diagnosed with solid tumors, B cell NHL, and multiple myeloma; no option for standard treatment; and adequate organ function; genomic test results from a CLIA certified, CAP accredited lab, NYS accredited. Investigators will group patients by tumor type-variant, with eight patients per group. If no treatment response is evident, those treatment groups will be disbanded. If at least one response is observable, researchers will enroll an additional 16 patients.

The study will be guided by ASCO®-Established Oversight Committees:

- Steering Committee to oversee the logistics (operations, publication policies, methods review);
- Molecular Tumor Board (MTB) to review the proposed drug-target match; and
- Data and Safety Monitoring Board (DSMB) to independently review the results, monitor adverse effects and if cohorts should be disbanded, and oversee data release.

A complete protocol will be submitted by July 2015; investigators hope to begin patient enrollment later this year.

Press Conference. June 1 2015.



Drugs: Revelations and Reflections

The advancement in drug therapy is perhaps the greatest priority for treating and seeking a cure for cancer. The three main therapies that generated the most discussion were the use of vaccinations to stimulate the immune system to attack cancer, the engineering of T-cells to assist them in recognizing and fighting cancer, and the control of TNF receptor agonists to stimulate the pathways for a more aggressive immune response.

Here are a few other facets of the discussion on drug therapy development.

3 Trends in Drug Development at a Glance

The conference presentations offered trends in oncology drug approval and development.

Drug approval and cost are always of interest to those researchers hoping to have success in clinical trials. Here are three studies offering insight.

HOW CAN BIOMARKERS AFFECT DRUG APPROVAL?

Study results offered in a paper title "A Decade of Oncology Drug Development," published in conjunction with the conference noted, "The FDA has been working to get efficacious and safe drugs quickly out to patients who would benefit from them...The number of oncology drug approvals has expanded greatly over the past decade, especially for solid tumors. The approval of monotherapy and biomarker-linked drugs in cancer increased two- and three-fold in the last decade, raising optimism that novel therapies may be shifting the approach towards treating oncologic malignancies."

CAN FINANCIAL CONFLICTS OF INTEREST AFFECT FDA DRUG APPROVAL?

A study titled "Association Between Oncologic Drugs Advisory Committee (ODAC) Members' Financial Conflicts of Interest (FCOIs) and Recommendations for Drug Approval by the U.S. Food and Drug Administration (FDA)" demonstrated that FCOIs, especially with the sponsor, are associated with higher odds of ODAC recommendation and of final FDA approval of oncologic drugs. The results showed that "voting members with any FCOIs were more likely to vote in favor of a drug (OR 1.34, p = 0.04). There was a near-significant interaction between the presence and type of FCOIs; FCOIs with the sponsor were associated with higher odds of voting in favor of a

Researchers found that drugs developed with a biomarker had success rates of 24% versus just 6% for those developed without biomarkers—a four-fold increase.

drug compared to FCOIs with a competitor (OR 1.89 vs. 0.97, interaction p = 0.052). Similar results were seen for the association of ODAC members' FCOIs and final FDA approval (OR 1.42, p = 0.03)."

HOW ARE PRICES IN DRUGS CHANGING OVER TIME?

An analysis titled "Price Migration of Oncology Drugs Launched in the United States between 2010 and 2015" similarly offered trends regarding the cost of these medications and treatments. The conclusion of the study showed "important differences in the magnitude and frequency of price increases taken by oncology drug manufacturers. Differences are seen by tumor type and by route of administration. Further inquiry may be useful to determine the structural and strategic factors driving these differences."

The Role of Biomarkers in Improving Clinical Trial Success: A Study of 1,079 Oncology Drugs

Biomarkers improve the chances of clinical trial success for cancer drugs, according to a paper spot-lighted in special issue of the *Journal of Clinical Oncology,* circulated as a session supplement at the conference.

Researchers from the University of Toronto noted that a large number of drug therapies have no success during clinical trial testing. Basing their study on a common belief that biomarkers can assist the chances of a compound advancing during drug development, investigators sought to perform "the most rigorous analysis of biomarker impact on cancer drug testing to date."

The authors focused on four indications (breast, lung, and colorectal cancer, and melanoma), pooling their data from the National Institutes of Health Clinical Trials database *(ClinicalTrials.gov)* and other publicly accessible information from January 1, 1998 to July 1, 2013. Using this data, screening over 10,000 clinical trials, they analyzed the presence or absence of biomarker use in conjunction with how far 1,079 drugs advanced.

Researchers found that drugs developed with a biomarker had success rates of 24% versus just 6% for those developed without biomarkers—a four-fold increase.

The increased success was most evident for phase III clinical trials for each disease studied.

While he was not opposed to the use of pain medicines, such as opioids, Dr. Campbell's focus was to offer alternative treatment to supplement other therapies—and, in some cases, replace drug therapy all together.

Reflections on the Challenges of Pain Management: Alternative Approaches

In an Extended Education session offered yesterday, panelists presented three key approaches in thinking about

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pain management for oncology patients: 1. Non-opioid Pain Medicines and Adjunctive Alternative; 2. Opioid Pain Medicines and Regulatory Issues; 3. Screening and Managing Misuse and Abuse.

The discussion offered by panelist **Toby Christopher Campbell, MD,** of the University of Wisconsin Cabrone Cancer Center, extended the drug discussion into the realm of supplemental treatment. He stressed that the key concern in pain management for cancer patients is their ability to maintain a relatively normal life. "What many of us hope is that our patients can function," he said. While making clear that he was not opposed to the use of pain medicines, such as opioids, his focus was to offer alternative treatment to supplement other therapies—and, in some cases, replace drug therapy all together.

Dr. Campbell argued that pain is much more than a physiological response, often decreasing quality of life (family, work, finances, etc.) and often changing behavior (psychological reactions to symptom, maladaptive responses). These additional concerns, as well as the substantial chronic pain cancer patients suffer, can benefit from alternative therapies: mind-body, movement, sensory art, and multi-modal integrative approaches.

While the aforementioned therapies are often guided, Dr. Campbell also noted there are many affordable, active self-care strategies such as meditation, yoga, homeopathic treatment, message, and using natural products.

Every patient is different and these alternative or complimentary therapies should be patient-centered, considering age, culture, education, readiness to change, outcome expectations, aptitude for specific strategies—and, of course, the type of pain, its intensity, and location.

Dr. Campbell did acknowledge the limited evidence for such therapies, as well as practitioner concern that may inhibit these treatments. ●

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