# THE CANCER LETTER

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## NCI-MATCH to Bring in Public, Private Funds, Giving NCI New Urgent Scientific Agenda

*By Paul Goldberg*

ECOG-ACRIN Cancer Research Group is starting enrollment in NCI-MATCH, the most ambitious of NCI's new generation of clinical trials.

In addition to being the centerpiece of the institute's recently formed National Clinical Trials Network, NCI-MATCH—the name is an acronym for Molecular Analysis for Therapy Choice—provides a strong case for garnering Congressional support for the White House precision medicine initiative.

(Continued to page 2)

*Conversation with The Cancer Letter*

## Doroshow: NCI-MATCH is an Example of What Smart Public-Private Partnerships Can Do

The NCI-MATCH phase II study is intended to allow the institute and its clinical trials groups catapult to the premier role in cancer research.

In a conversation with The Cancer Letter, James Doroshow, director of the NCI Division of Cancer Treatment and Diagnosis, said NCI-MATCH established the institute as a trusted party in a complex, multi-agent trial intended to produce leads for government-funded investigators and pharma companies would be able to follow.

On the public side, NCI-MATCH provides an example of what NCI will be able to do with the $70 million proposed under President Obama's Precision Medicine Initiative. New NCI funding is included in the White House budget proposal for 2016, but it's up to Congress to appropriate these funds.

"If Congress appropriates the $70 million to NCI as proposed in the president's Precision Medicine Initiative, we would allocate those resources for pursuing additional research based on patient responses to the therapies used in the trial," Doroshow said to The Cancer Letter. "Under the president's initiative, if funded, we hope to use early signals from NCI-MATCH to direct new trials, and develop other precision medicine priorities under an initiative we are calling NCI-MATCH+."

(Continued to page 5)

## ASCO CEO Lichter to Step Down in June 2016

Allen Lichter, CEO of the American Society of Clinical Oncology and the Conquer Cancer Foundation of ASCO, announced June 1 that he would step down June 30, 2016.

Lichter has led ASCO since 2006.

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## NCI-MATCH Trial Begins; Will New Money Follow?

(Continued from page 1)

The $215 million program proposed by Obama as part of appropriations for fiscal 2016 hasn't translated into congressional appropriations. The PMI budget request includes $70 million for NCI to scale up efforts to identify genomic drivers in cancer and apply that knowledge to develop more effective approaches to cancer treatment. Similarly, the new-generation trials would boost the NCI case in pursuit of a share of another potential windfall: the 21st Century Cures.

"We hope to—if we are fortunate enough to receive the resources that have been requested from Congress—to be able to leverage this particular trial as well as our other precision medicine trials to develop NCI-MATCH-like studies in which we can go deeper into particular diseases based on the early signals we get from this investigation," said James Doroshow, director of the NCI Division of Cancer Treatment and Diagnosis.

Doroshow spoke at the June 1 press conference at the annual meeting of the American Society of Clinical Oncology, where NCI-MATCH was unveiled. His conversation with The Cancer Letter appears on p. 1.

NCI-MATCH has the potential to capture the attention of the public—and their elected representatives—because it will do something no large nationwide study has done before: assign patients to therapy based on genetic characteristics—as opposed to the site—of their tumors.

Accrual in the phase II NCI-MATCH trial will start in July. As it opens, the trial will have 10 arms, with plans to increase that number to 20 or more in a matter of months.

For the research groups that make up NCI's National Clinical Trials Network, new money would deliver on a promise that was made when the institute started to consolidate the nine cooperative groups focused on adult cancer to create four adult groups and one pediatric group.

Originally, the plan was to add $25 million to the system to make it possible to increase payment for each patient placed in a clinical trial. However, the money didn't come through and the number of patients enrolled in trials was reduced. Also, group chairs said that over $20 million was cut out of the groups' operations and statistical centers (The Cancer Letter, May 16, 2014). Overall, funding for the groups remained flat.

The trial is led by ECOG-ACRIN, but is open for enrollment from all adult NCTN groups. For ECOG-ACRIN, NCI-MATCH represents an opportunity to revolutionize cancer care.

"It's an unprecedented approach through the clinical trials system," Robert Comis, ECOG-ACRIN co-chair, said to The Cancer Letter. "Obviously, NCI-MATCH is disease-agnostic, and we are going to be putting patients on the study based upon the mutations and abnormalities we find in their tumors."

It could very well turn out that in some cases the origin of the tumor will be important while in others it will be irrelevant.

"We won't know until we get into this," Comis said. "What we know from all of the experiences to date is that there are certain abnormalities like HER2 that are present and actionable in both breast and stomach cancers. Then there are other abnormalities like BRAF inhibitors and BRAF-V600E that work in melanoma, but don't really appear to work in colon cancer.

"But what is so unprecedented about NCI-MATCH is that we have established an incredibly well-coordinated laboratory network and operational infrastructure specifically for this trial that will implement our targeted sequencing approach with great precision and accuracy that we have proven has a concordance rate of 96-100 percent. And so, if we see an agent working against a particular variant or mutation, we will be very certain that we have hit that target. The laboratory support component of this is really tremendous."

Comis said the group has received a financial supplement from NCI, but has invested a great deal more to create the NCI-MATCH infrastructure. "We received some supplemental money to support all the work that this required, but it clearly didn't cover what

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was needed to do the work," Comis said to The Cancer Letter.

"It's hard to know precisely, but we have a large number of FTEs in ECOG-ACRIN working on this trial," Comis said. "If we receive enough precision medicine money from the government, it will become a key component of what is needed to support our people. We can all keep our fingers crossed."

NCI-MATCH will enroll patients with advanced solid tumor or lymphoma refractory to standard therapy. The goal is to include 25 percent of patients with rare cancers. The trial will screen about 3,000 patients for genetic abnormalities and assign about 1,000 of them to treatment arms, which will include approximately 35 patients each. The study will have 2,400 participating sites. To participate, sites must be part of the NCI Central IRB.

NCI-MATCH's primary endpoint is tumor response to treatment, defined as tumor shrinkage of 30 percent or more over a defined period of time. Treatments will be considered promising if 16 percent to 25 percent of the patients in an arm have tumor shrinkage, and will be considered unsuccessful if less than 5 percent have tumor shrinkage

NCI-MATCH will also assess progression-free survival. A treatment will be considered promising if a PFS of six months or longer is seen in 35 percent of the patients treated with that drug, and will be considered unsuccessful if only 15 percent of the patients have a PFS of six months or longer.

Patients whose cancers progress during the first assigned treatment may be able to go onto another NCI-MATCH arm if they are found to have a second molecular target for which a drug is being studied. Any patient whose cancer initially shrinks and later progresses during the trial will be eligible to have a repeated biopsy. Time to progression will also be assessed.

A list of the first ten compounds appears in the table.

*Source:* www.cancer.gov

| Drug(s) | Molecular Target(s) | Estimated Mutation Prevalence |
|---|---|---|
| Crizotinib | ALK rearrangement | 4% |
| Crizotinib | ROS1 translocations | 5% |
| Dabrafenib and Trametinib | BRAF V600E or V600K mutations | 7% |
| Trametinib | BRAF Fusions/ Non-V600E/Non-V600K BRAF mutations | 2.80% |
| Afatinib | EGFR activating mutations | 1-4% |
| Afatinib | HER2 activating mutations | 2-5% |
| AZD9291 | EGFR T790M mutations and rare EGFR activating mutations | 1-2% |
| Ado-trastuzumab emtansine | HER2 amplification | 5% |
| VS6063 | NF2 loss | 2% |
| Sunitinib | cKIT mutations | 4% |

**A Single Targeted Sequencing Assay Platform**

The science is worth the risk, Comis said.

By asking a fundamental question—the relevance of organ-sites—NCI-MATCH could re-establish NCI and its publicly funded clinical trials infrastructure as the catalyst of innovation in oncology.

"That's why we are so interested and committed to NCI-MATCH. The FDA reviewed our next-generation sequencing device along with the IND submission, and gave permission to proceed with the diagnostic for investigational use in the trial—which is unprecedented for cancer," Comis said. "The laboratory people worked incredibly hard to provide the data validating the accuracy and reproducibility of this assay, which tests for multiple cancer related genetic aberrations at once. This is a tremendous achievement."

Doroshow agrees. "We think that doing that will help change the entire paradigm for cancer clinical trials and will also allow us to collect—through the biopsies that are a part of this program—the kinds of materials that will fundamentally allow us to use clinically annotated information from those biopsies the get a much better understanding of how we can go about understanding both tumor heterogeneity and resistance to novel therapies," he said at a press conference at the ASCO annual meeting.

The trial requires massive infrastructure and would be hard to duplicate in the private sector:

• **At the heart of the trial is a targeted sequencing assay** that was originally designed at NCI. "I thought this was going to be one of the most challenging hurdles of developing this trial: Getting the FDA to agree to a targeted sequencing assay. Now, with the FDA determination, the targeted sequencing assay puts the public system at a great advantage." Comis said.

The assay examines the specimen for more than 4,000 variants across 143 genes. The test was developed at the NCI Molecular Characterization Laboratory at the NCI Frederick National Laboratory for Cancer Research in Frederick, Md.

• **The ECOG-ACRIN Central Biorepository and Pathology Facility at MD Anderson Cancer Center** will process biopsies from all 3,000 screened patients to ensure concordance in testing. The sequencing analysis will be done at one of four facilities using a standardized process. These are: MD Anderson Cancer Center Molecular Diagnostics NGS Laboratory; Massachusetts General Hospital Center for Integrated Diagnostics; Molecular Characterization Laboratory at the NCI Frederick National Laboratory for Cancer Research, operated by Leidos Biomedical Research Inc.; and Yale University Tumor Profiling Laboratory.

"It starts with all specimens being sent in a unique collection kit to our ECOG-ACRIN Central Biorepository and Pathology Facility at MD Anderson," Comis said. "Once Stan Hamilton's staff processes the specimens, they will go out to the four chosen CLIA labs for sequencing. You can't have a precision medicine approach without a precision diagnostic. The key to all of this is that the concordance rate across the different variants (96 to 100 percent) was much better than expected. They've done a tremendous amount of work to make this happen."

• **A unique specimen collection kit.** The group designed a specialized specimen collection kit that you can learn more about. This goes out to the sites.

• **NCI will pay for biopsies and genetic testing**—up to $3,000 per biopsy for a maximum of five biopsies. "The government will pay for it, which is another selling point for its success in the field," Comis said. "And then we get the usual payments for case reimbursement and additional tests. We are working on the actual details of the budget right now." The device manufacturer for the DNA analytics is Thermo Fisher Scientific Inc. The device employs a targeted sequencing approach using Ion Torrent next-generation sequencing technology

• **A tool called NCI-MATCH Box** will be used to assign patients to therapy based on their tumor characteristics. It will be making the calls on what mutations are there. And then that information is forwarded to ECOG-ACRIN through the CTSU and all the IT pipes that were established between our operations center and the central biorepository and pathology facility at Anderson.

• **A central IRB** will bypass the IRBs at the 2,400 participating sites. "This can't be done without a central IRB," Comis said. "It's just too complicated for the sites to handle on their own. To participate in NCI-MATCH, the sites are going to have to be part of the NCI Central IRB and that's something we've all worked for over the years and now it's become part of the process."

• **Data will be collected through the** Medidata Rave system and used uniformly through the NCI clinical trials infrastructure.

NCI-MATCH will have a pediatric counterpart that will enroll children with advanced cancers that have progressed on standard therapy. The institute's objective is to make the same drugs available in both the adult and pediatric versions of NCI-MATCH.

The pediatric trial, which is a component of the NCI FY 2016 budget, will be led by the NCI-supported NCTN Children's Oncology Group.

Other similar NCI trials include:

• Exceptional Responders Initiative, which seeks to learn why a minority of patients with solid tumors or lymphoma respond very well to some drugs even if the majority do not;

• ALCHEMIST trial, which seeks to learn whether targeted epidermal growth factor receptor and anaplastic lymphoma kinase inhibitors improve survival for adenocarcinoma of the lung in the adjuvant setting.

• Lung Cancer Master Protocol trial for advanced squamous cell lung cancer, which seeks to show whether there an advantage to developing drugs for small subsets of molecularly characterized tumors in a single, multi-arm trial design.

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**Correction:** A previous version of this story stated that the multi-gene diagnostic to be used in NCI-MATCH was "FDA-approved." The targeted assay has, in fact, been determined by the FDA to be a non-significant risk medical device for investigational use only. NCI held two pre-submission meetings with the FDA Center for Devices and Radiological Health to discuss appropriate analytic validation. The assay will be used in accordance with abbreviated IDE requirements.

*Conversation with The Cancer Letter*

# Doroshow: NCI-MATCH Trial to Be Followed by NCI-MATCH+

(Continued from page 1)

NCI-MATCH has generated considerable excitement in the pharma industry, Doroshow said.

Pharma companies have "shown an ongoing, strong interest in the subsequent studies that could be conducted under NCI-MATCH+, and of course, it's through their involvement that we'll see better treatments for patients," Doroshow said. "We currently have signed agreements with over 20 pharmaceutical companies to contribute over 40 drugs to the study, which provides a very comprehensive pharmacopeia.

"Additionally, during the ASCO annual meeting this past week in Chicago, we met with interested pharmaceutical companies beyond those with whom we have agreements; there was a considerable amount of interest, and we hope to develop an even greater drug library as the trial progresses."

Doroshow spoke with Paul Goldberg, editor and publisher of The Cancer Letter.

**Paul Goldberg:** *This has the look of something that will keep The Cancer Letter busy for years to come. How is NCI-MATCH different from all the other trials?*

**Jim Doroshow:** NCI-MATCH is the largest trial to date in oncology to determine systemic cancer treatment based on the molecular characteristics of a cancer, including specific mutations, instead of its tissue of origin.

Let me outline a few ways that the trial is unique:

• NCI-MATCH was developed by literally hundreds of specialized clinical investigators and scientists working in NCI-supported clinical trial networks (National Clinical Trials Network, NCI Community Oncology Research Program, and Experimental Therapeutics-Clinical Trials Network) and cancer centers, as well as NCI staff, who are at the cutting edge of precision oncology, with input from community oncologists and patient advocates.

The ECOG-ACRIN clinical trials group, one of five groups comprising the NCTN, is coordinating the study and has played a critical role, together with NCI, in developing a novel information technology platform that is used to make treatment decisions following molecular tumor characterization. ECOG-ACRIN has also worked extraordinarily hard to integrate the complex information flow needed to provide clinical trial sites with the data required to initiate treatment in this study. The degree of collaboration and coordination needed to develop all phases of NCI-MATCH across the entire cancer community has, in my opinion, been unprecedented.

• All genetic testing of patient tumor samples in NCI-MATCH will be performed using a rigorously-standardized process in one of four Clinical Laboratory Improvement Amendments-certified laboratories to make certain that the molecular characterization results are the same wherever the sample is analyzed.

The four laboratory sites are: MD Anderson Cancer Center Molecular Diagnostics Next Generation Sequencing Laboratory; Massachusetts General Hospital Center for Integrated Diagnostics; Molecular Characterization Laboratory at the NCI Frederick National Laboratory for Cancer Research; and Yale University Tumor Profiling Laboratory.

The investigators in the chosen laboratories are among those with the most expertise in these types of assays. The testing also uses highly standardized procedures for the collection of tumor samples and for preparing the samples for analysis.

• Importantly, because cancer is a disease that continues to change over the course of time, new tumor samples must be obtained prior to consideration for entry in the NCI-MATCH trial. Archived specimens will not be used to determine patient eligibility. Patients must have received standard treatment that is no longer effective to be eligible for NCI-MATCH.

• The NCI is serving as a 'safe harbor' for the development of a large portfolio of drugs from many companies that are suitable for use against the wide range of mutations that will be studied in the NCI-MATCH trial. Many pharmaceutical companies are collaborating in NCI-MATCH by contributing both drugs and their expertise. This is possible because of the unique position of the NCI with respect to its ability to work with many commercial firms without interfering with their intellectual property positions.

We currently have signed agreements with over 20 pharmaceutical companies to contribute over 40 drugs to the study, which provides a very comprehensive pharmacopeia. Additionally, during the ASCO annual meeting this past week in Chicago, we met with interested pharmaceutical companies beyond those with whom we have agreements; there was a considerable amount of interest, and we hope to develop an even greater drug library as the trial progresses.

• NCI-MATCH is an umbrella trial that is designed to initially encompass 20 or more individual phase II studies, each matching specific drugs or drug combinations to a specific mutation in a tumor. The

advantage of this novel trial design is that it allows us to initiate new studies (of new drug/mutation pairs) easily as new data arises, as well as to perform confirmatory studies of new therapeutic signals under the NCI-MATCH umbrella. This trial also allows us to utilize our entire network, from community doctors who participate in NCORP to those with large clinical facilities at teaching hospitals, to screen patients for mutations that may be rare.

To my knowledge, this is the first time that a trial of this size, which is histologically-agnostic with respect to tumor type, has been attempted.

**PG:** *My second question is a crass question: What is your budget for NCI-MATCH?*

**JD:** We have currently budgeted about $30-40 million for the trial. However, it is difficult to estimate the degree of response we will observe in each of the sub-studies—thus, the budget could certainly expand.

If Congress appropriates the $70 million to NCI as proposed in the president's Precision Medicine Initiative, we would allocate those resources for pursuing additional research based on patient responses to the therapies used in the trial. Under the president's initiative, if funded, we hope to use early signals from NCI-MATCH to direct new trials, and develop other precision medicine priorities under an initiative we are calling NCI-MATCH+.

**PG:** *We know the start date; what's the end date? How does it end, and where will we be when it ends?*

**JD:** To be clear, we expect to enroll the first patients in NCI-MATCH next month. That will be the true start of the trial. The formal end is specified in the trial protocol and is based on screening about 3,000 patients to enroll about 1,000 patients in the various treatment arms. Each arm will include approximately 35 patients. So when those accrual goals are met, that is the pre-specified end of enrollment.

But, we would certainly like to take advantage of the structure of the trial to expand it if we find something in a particular sub study that is exciting. To be more specific, if one of the arms was successful, we could go beyond 35 patients to an expanded phase II trial of perhaps 50-100 patients. The next step after that would be a randomized phase III study, which might be something that investigators in the NCTN would be interested in pursuing. We certainly have the structure set up to amend a trial as it progresses.

**PG:** *This is phase II, not big cohorts; it's not randomized. So there will be spinoff studies for successful compounds, yes? How would that work? Would these be drug company studies or NCTN studies?*

**JD:** All of the arms will be initiated as sub studies under NCI-MATCH. But the data from the sub studies will be shared with the firms who contributed the drugs. I could foresee additional studies being supported either by the NCI or by a pharmaceutical partner.

**PG:** *How were the first 10 compounds picked? What happens when an arm falls off? Will a new arm replace it? How will that arm be picked?*

**JD:** The process has been iterative and rigorous. First, we formed a committee to decide which genes would make the best targets. Then a group of extramural investigators were invited to review the currently available commercial and investigational drugs to determine, using pre-specified levels of evidence, which ones could target the selected genes. Then, technology transfer staff in my office spent a good deal of time negotiating contracts with drug companies.

Ultimately, the process became self-reinforcing, with a useful feedback loop whereby we were able to consider new genes, new drugs, and possible choices for new arms in an accelerated fashion.

In the trial, once a patient is enrolled, if their disease progresses during the first assigned treatment, they may be able to go on another NCI-MATCH trial arm if they have a second molecular target in their tumor (after having another biopsy) that can be treated with an available drug. Any patient whose cancer initially shrinks and later progresses has the same opportunity to have their tumor re-biopsied and to enroll in one of the other treatment arms if a slot is available.

If there is no tumor reduction seen (and overall response rate is our primary endpoint, with progression-free survival being a secondary endpoint) in any specific sub-study, the study will close. We have very clear stopping criteria. New arms are continuously under consideration as we identify new putative targets and determine whether there are drugs that might be appropriately used against those targets.

**PG:** *Do you expect to get funds from the president's Precision Medicine Initiative? How much can you spend?*

**JD:** Congress is the ultimate voice on funding. We are hopeful that there will be funding for the Precision Medicine Initiative, and we have a plan to use those funds to build on the NCI-MATCH study and undertake new precision medicine research should funds be appropriated by Congress.

**PG:** *What can NCTN groups—which say that they have felt considerable pain in recent years—hope to gain?*

**JD:** We are very appreciative of the considerable time and effort that all of the NCTN partners have put

into this remarkable project. They have been at the table as the protocol was developed and the information technology evolved, which required a lot of dedicated time and technical effort on everyone's behalf. An enormous number of investigators, researchers, physicians, health care professionals, and advocates have helped to develop the infrastructure necessary to make this trial a reality. The success of this study, which utilizes all of the strengths of the NCTN, will demonstrate the considerable capability of the network to perform the most innovative clinical trials.

We would be remiss, of course, if we did not again give special thanks to ECOG-ACRIN, which is coordinating the trial. The other adult trial groups in the NCTN—the Alliance for Clinical Trials in Oncology, SWOG, and the NRG Oncology Group—have all collaborated significantly in the development of NCI-MATCH.

**PG:** *Will there be new NCI money following this initiative? New pharma money?*

**JD:** Based on the enthusiasm we're hearing from the cancer research community about this approach, we're optimistic that the Precision Medicine Initiative will bring funds to NCI-MATCH and allow us to pursue the potential of NCI-MATCH+, but in the end that's entirely up to Congress to decide.

In the meantime, we definitely appreciate the support and enthusiastic participation we are hearing and seeing from our pharmaceutical and device partners.

At the core, this trial is a terrific example of what can come from a well-conceived and designed public-private partnership. As for new pharma money, we cannot speak about their budgets, but so far they've shown an ongoing, strong interest in the subsequent studies that could be conducted under NCI-MATCH+, and of course, it's through their involvement that we'll see better treatments for patients.

**PG:** *Please correct me if I am veering in the direction of silly, unbridled optimism, but do you see this initiative putting NCI back in the nerve center of the drug development program at a new, scientifically relevant level?*

**JD:** NCI-MATCH demonstrates the extraordinary power of collaboration between academia, pharma, community oncologists, NCI, and others. It is this partnership that has made it possible to inaugurate this study.

My hope is that this trial will demonstrate the feasibility of a new paradigm for the development of molecularly targeted therapeutics and will serve as a model for our Pediatric NCI-MATCH, due to launch next year. In support of this new paradigm, we believe that NCI can serve to make resources available to energize the cancer research community to collaborate in the completion of the most innovative clinical trials for our patients.

## Melanoma Drugs Could Be Used To Treat Lung, Liver, Head-Neck And Colorectal Cancers

Three immunotherapy drugs approved for the treatment of melanoma may be used to treat advanced lung, liver, head and neck, and colorectal cancers, according to clinical trial results presented at the 2015 American Society of Clinical Oncology annual meeting in Chicago.

These drugs—Keytruda (pembrolizumab) by Merck, and Opdivo (nivolumab) and Yervoy (ipilimumab) by Bristol-Myers Squibb—are called checkpoint inhibitors because they release the molecular checkpoints that keep the immune system from attacking tumors.

FDA approved Opdivo in March as second-line treatment for advanced squamous non-small cell lung cancer.

The studies presented were:

A randomized phase III study, which established Opdivo as a possible standard second-line treatment option for non-squamous non-small cell lung cancer.

A phase I/II study that identified a potential new role for Opdivo in advanced liver cancer,

A small study that identified a potential role for Keytruda in patients with head and neck cancer.

A phase II study, which demonstrated that a specific genomic abnormality called mismatch repair (MMR) deficiency predicts response to Keytruda. This marker predicted responses in patients with colorectal, endometrial and several other types of cancer.

A randomized phase III trial for patients with melanoma, which found that Opdivo alone or in combination with Yervoy is significantly more effective than Yervoy alone.

**Opdivo in Non-Squamous NSCLC**

A randomized phase III study (CHECKMATE-057) demonstrated that PD-1 immunotherapy is an effective treatment option for patients with non-squamous, non-small cell lung cancer.

Among patients with advanced disease that worsened after receiving platinum-based chemotherapy, those treated with Opdivo lived on average three months

# CheckMate 057 (NCT01673867) Study Design

- Stage IIIB/IV non-SQ NSCLC
- ECOG PS 0–1
- 1 prior PT-DC
- Prior maintenance therapy with pemetrexed, bevacizumab, or erlotinib allowed[a]
- Prior TKI therapy allowed for known *ALK* translocation or *EGFR* mutation

N=582

Randomize 1:1

**Nivolumab**
3 mg/kg IV Q2W until PD or unacceptable toxicity
N=292

**Docetaxel**
75 mg/m² IV Q3W until PD or unacceptable toxicity
N=290

**Primary Endpoint**
- OS

**Additional Endpoints**
- ORR[b]
- PFS[b]
- Safety
- Efficacy by tumor PD-L1 expression
- Disease-related symptom improvement rate by week 12

- Pts stratified by prior maintenance therapy and line of therapy (second- vs third-line)
- PD-L1 expression was measured in pre-treatment (archival or recent) tumor biopsies using the Dako automated IHC assay
- The Dako/BMS PD-L1 assay is fully validated with analytical performance having met all pre-determined acceptance criteria for sensitivity, specificity, precision, and robustness[1,2]

[a] Not considered a separate line of therapy; [b] Per RECIST v1.1 criteria as determined by the investigator.
1. Rizvi et al. Lancet Oncol 2015;Mar;16:257-65. doi: 10.1016/S1470-2045(15)70054-9. Epub 2015 Feb 20; 2. Brahmer et al. N Engl Med 2015 (in press).

*ALK* = anaplastic lymphoma kinase; ECOG PS = Eastern Cooperative Oncology Group performance status; *EGFR* = epidermal growth factor receptor; IHC = immunohistochemistry assay; IV = intravenous; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PD = progressive disease; TKI = tyrosine kinase inhibitor

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PRESENTED AT: ASCO Annual '15 Meeting

# Objective Response Rate

| | Nivolumab (N = 292) | Docetaxel (N = 290) |
|---|---|---|
| ORR (95% CI) | 19% (15, 24) | 12% (9, 17) |
| *Odds Ratio* (95% CI)<br>*P*-value[a] | 1.72 (1.1, 2.6)<br>0.0246 | |
| Best overall response, %<br>CR<br>PR<br>SD<br>PD<br>Unable to determine | <br>1<br>18<br>25<br>44<br>11 | <br><1<br>12<br>42<br>29<br>16 |
| Median time to response,[b] mos (range) | 2.1 (1.2, 8.6) | 2.6 (1.4, 6.3) |
| Median DOR,[b] mos (range) | 17.2 (1.8, 22.6+) | 5.6 (1.2+, 15.2+) |
| Ongoing response,[c] % | 52 | 14 |

- 71 (24%) pts on nivolumab were treated beyond RECIST v1.1-defined progression
- Non-conventional benefit was observed in 16 pts (not included in best overall response)

[a] Based on two-sided stratified Cochran Mantel Haenszel test; [b] Values are for all responders (nivolumab, n = 66; docetaxel, n = 36); [c] Ongoing response at last tumor assessment before censoring. Symbol + indicates a censored value.

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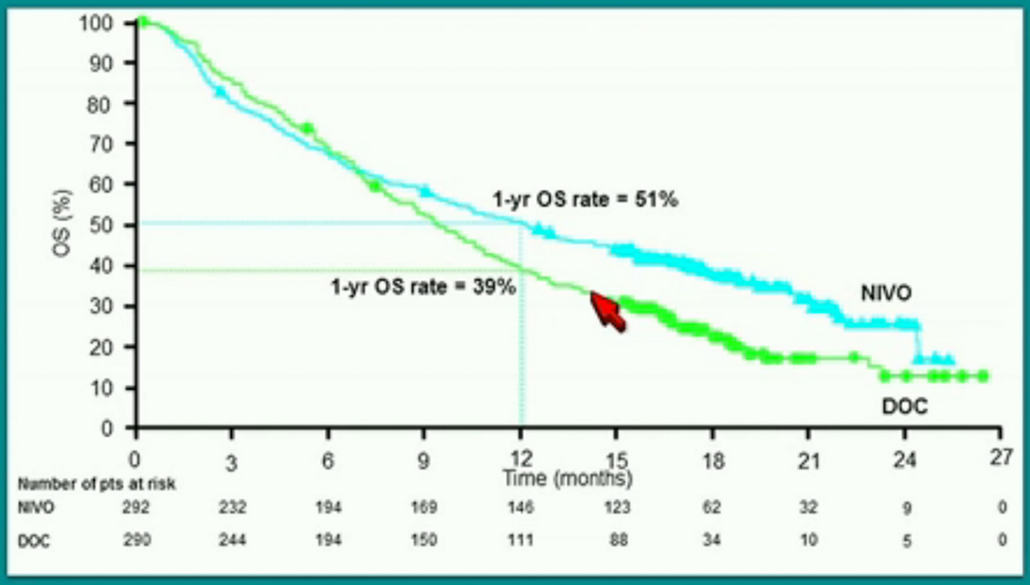
PRESENTED AT: ASCO Annual '15 Meeting

# Overall Survival




**Minimum follow-up for OS was approximately 13.2 mo**

Symbols represent censored observations.
CI = confidence interval; HR = hazard ratio

PRESENTED AT: ASCO Annual '15 Meeting

# Treatment and Safety Summary

| | Nivolumab N = 287 | | Docetaxel N = 268 | |
|---|---|---|---|---|
| Median number of doses received (range) | 6 (1, 52) | | 4 (1, 23) | |
| Relative dose intensity, ≥90% | 83 | | 66 | |
| Pts continuing treatment, % | 15 | | 0 | |
| Pts who received subsequent systemic therapy, % | 42 | | 50 | |
| | Any Grade | Grade 3–4[a] | Any Grade | Grade 3–4[a] |
| Treatment-related AEs, % | 69 | 10 | 88 | 54 |
| Treatment-related SAEs, % | 7 | 5 | 20 | 18 |
| Treatment-related AEs leading to discontinuation, % | 5 | 4 | 15 | 7 |
| Treatment-related deaths, % | 0[b] | | <1[c] | |

[a] No grade 5 events were reported at DBL; 1 grade 5 event was reported for nivolumab post-database lock [b]; 1 death attributed to nivolumab (encephalitis); association to nivolumab changed after DBL; [c] 1 death attributed to docetaxel-related drug toxicity; grade 4 febrile neutropenia.

32 AE = adverse event

PRESENTED AT: ASCO Annual '15 Meeting

longer than those treated with docetaxel chemotherapy.

"This is the first phase III study to show that immunotherapy is effective against non-squamous cell NSCLC, and appears to be particularly active in patients with PD-L1-positive tumors," said lead study author Luis Paz-Ares, professor of medicine at Hospital Universitario 12 de Octubre in Madrid, Spain. "While Opdivo appears to be more potent against this most common lung cancer, it is important to note that it is also far easier on patients compared to the standard second-line treatment, docetaxel."

The study randomly assigned 582 patients with advanced non-squamous NSCLC to treatment with Opdivo or docetaxel. Response rates were higher in the Opdivo group compared to the docetaxel group (19.2 percent vs. 12.4 percent). Responses also lasted significantly longer in the Opdivo group (17.1 months vs. 5.6 months, on average).

The median overall survival was 12.2 months in the Opdivo group compared to 9.4 months in the docetaxel group. In the subgroup of patients with high levels of PD-L1 in their tumor (≥1 percent cells), the median survival with Opdivo exceeded 17 months, compared to 9 months for those treated with docetaxel.

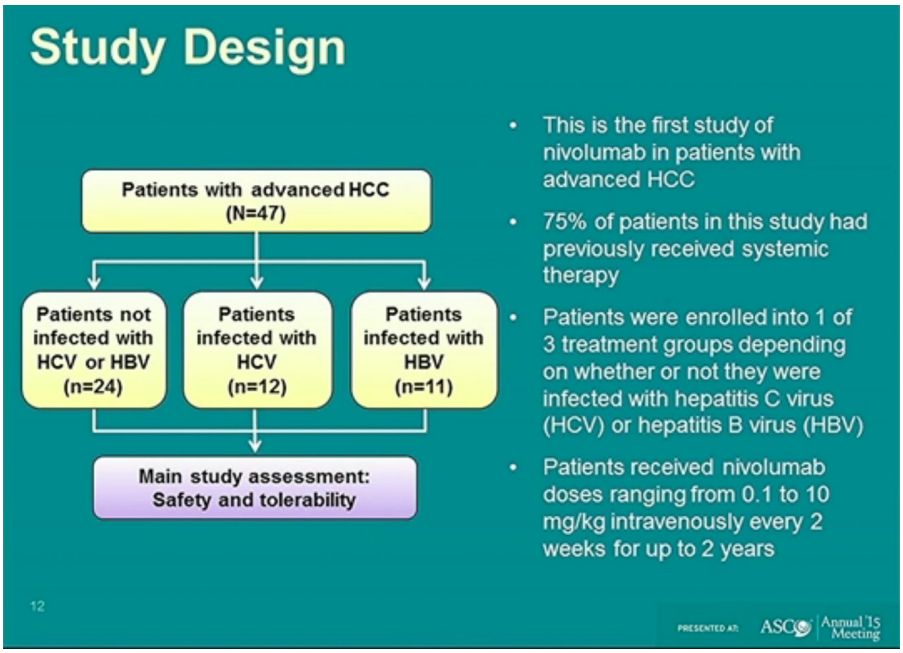
Opdivo was well tolerated overall, with only one in 10 patients experiencing serious side effects, compared to more than half of patients in the docetaxel arm. There was one treatment-related death in the docetaxel arm and none in the Opdivo arm. Due to toxic side effects, 4.9 percent patients stopped Opdivo, and 14.9 percent patients stopped docetaxel.

Nearly half of the patients who stopped treatment subsequently received systemic therapy.

The researchers pointed out that patients with higher levels of the biomarker PD-L1 experienced the greatest degree of benefit from Opdivo. Overall, patients who received Opdivo had a 27 percent lower risk of death compared to those who received docetaxel.

However, the subgroup of patients with the high levels of PD-L1 had a 41 to 60 percent reduction in risk of death, which was not observed in cases of low or undetectable PD- L1 levels.

## Opdivo in Advanced Liver Cancer




**Opdivo in Advanced Liver Cancer**

Findings from a phase I/II study suggest that Opdivo is safe and effective in advanced liver cancer. Based on the results of the phase I part of the study, eight (19 percent) of the 42 evaluable patients responded to the anti-PD-1 antibody with tumor reduction beyond 30 percent.

More importantly, the responses have been durable and surpassed 12 months in four patients. The overall survival rate at 12 months was 62 percent.

There is currently only one FDA-approved systemic treatment for advanced liver cancer: the multi-targeted tyrosine kinase inhibitor, sorafenib. However, just 2 percent of patients have an objective tumor response (more than 30 percent shrinkage) to sorafenib, and the average overall survival is 10 to 11 months.

"We are encouraged to see that Opdivo was safe overall, and the response rate as well as preliminary survival data look quite promising," said lead study author Anthony El-Khoueiry, an associate professor of clinical medicine and phase I program director at the University of Southern California Norris Comprehensive Cancer Center. "While we have to verify this early signal in larger studies, this is one of the first signs that immunotherapy with immune checkpoint inhibitors will have a role in the treatment of liver cancer."

Seventy-five percent of the patients enrolled on the study had previously received systemic therapy, including 68 percent who had received sorafenib.

## Opdivo in Advanced Liver Cancer

# Preliminary Safety With Nivolumab

| | Total Patients (N=47) | |
|---|---|---|
| | Any Grade | Grade 3–4 |
| Patients with any treatment-related adverse event, % | 68 | 19 |
| Treatment-related adverse events reported in ≥10% of patients | | |
| Aspartate aminotransferase increased | 19 | 11 |
| Lipase increased | 17 | 9 |
| Rash | 17 | 0 |
| Alanine aminotransferase increased | 15 | 9 |
| Amylase increased | 15 | 0 |
| Pruritus | 13 | 0 |

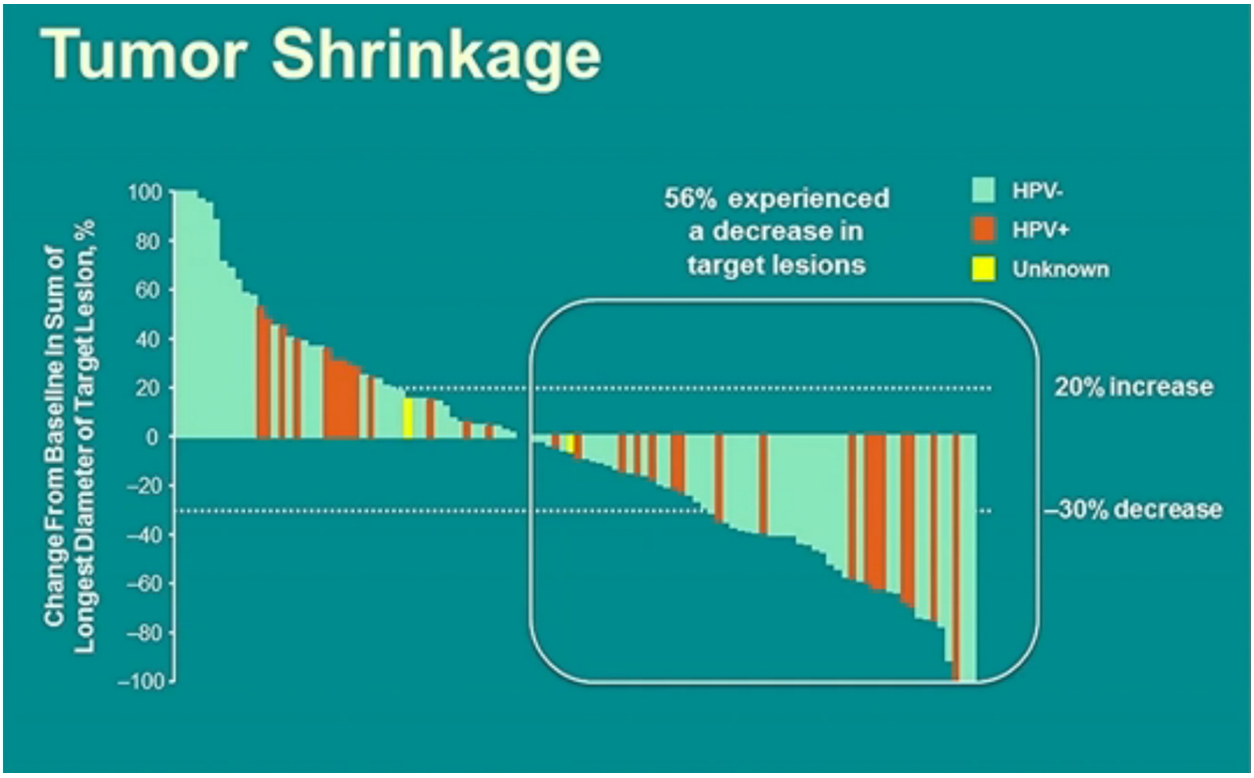
- 47 patients were treated in the study as of March 12, 2015
- No maximum-tolerated dose of nivolumab has been identified in this study
- The safety profile of nivolumab in this study is generally consistent with that previously reported with nivolumab in other types of cancer
- There were no deaths related to treatment

# Preliminary Anti-Tumor Response and Overall Survival With Nivolumab

| | Uninfected (n=21) | HCV (n=11) | HBV (n=10) | Total Patients Evaluable (n=42) |
|---|---|---|---|---|
| Objective response rate, n (%) | 3 (14) | 4 (36) | 1 (10) | 8 (19) |
| Complete response | 2 (10) | 0 | 0 | 2 (5) |
| Partial response | 1 (5) | 4 (36) | 1 (10) | 6 (14) |
| Ongoing response, n (%) | 3/3 (100) | 3/4 (75) | 0 | 6/8 (75) |

- Eight (19%) patients achieved complete or partial response, meaning that the size of their tumors measured at baseline decreased by 30%–100% with nivolumab treatment
  - Responses were observed in patients with hepatitis B or C viral infections as well as those who were uninfected
  - Responses were seen early during treatment and have continued in the majority of patients
- 62% of patients in the study were still surviving with HCC at 12 months

## Keytruda in Head and Neck Cancer




Opdivo was given intravenously every two weeks for up to two years.

The overall response rate was 19 percent, with eight patients experiencing objective tumor shrinkage beyond 30 percent, and two having complete remissions. The responses were durable, with 50 percent lasting beyond 12 months as most patients continued on treatment.

In addition, tumor growth was stalled in 48 percent of patients, with the longest case lasting beyond 17 months.

Opdivo was safe and well tolerated, even in patients with ongoing hepatitis B or C infections. The majority of the side effects were mild to moderate in nature with abnormal liver enzymes, rash, and elevation of amylase and lipase being the most common; the abnormal liver enzymes and elevated amylase and lipase were not accompanied by any significant clinical symptoms.



**Keytruda in Head and Neck Cancer**

A 132-patient study indicates that Keytruda immunotherapy is effective for patients with recurrent or metastatic head and neck cancer. The findings may fill a large unmet need for better treatments in this disease.

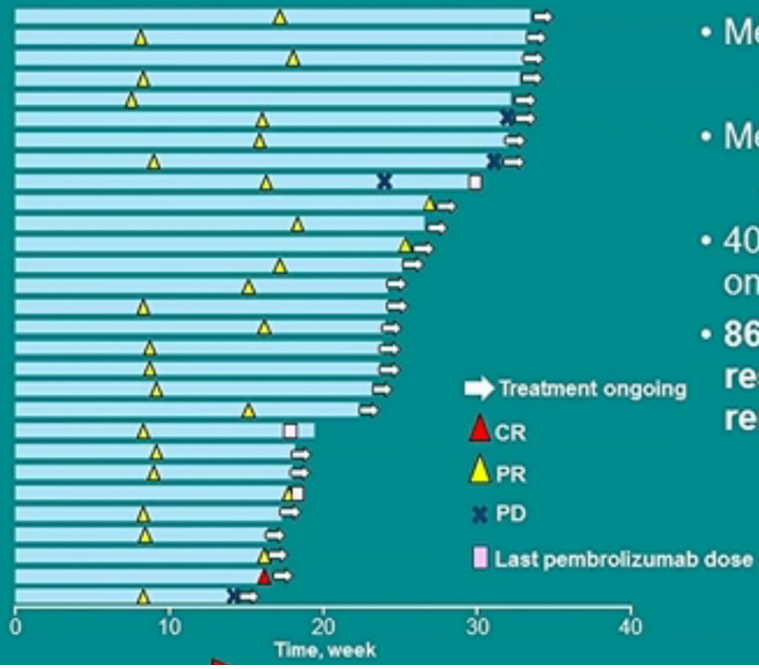
Overall, 57 percent of patients experienced some tumor shrinkage, and 24.8 percent had a marked decrease in tumor size known as partial or complete response. Keytruda was active across a wide range of patient subgroups including those with HPV-positive and HPV-negative HNC.

"The efficacy we saw was remarkable—Keytruda seems to be roughly twice as effective, when measured by response, as our only targeted therapy cetuximab," said lead study author Tanguy Seiwert, an assistant professor of medicine, and associate HNC program leader at the University of Chicago. "Unlike EGFR-inhibitors, where data at this meeting suggest potentially less efficacy in HPV-positive tumors, Keytruda showed similar levels of activity in both HPV-positive and HPV-negative tumors."

Standard initial treatment involves platinum based doublet chemotherapy with or without cetuximab, the only approved targeted therapy for HNC. Second-line options include methotrexate, docetaxel, and cetuximab.

## Keytruda in Head and Neck Cancer

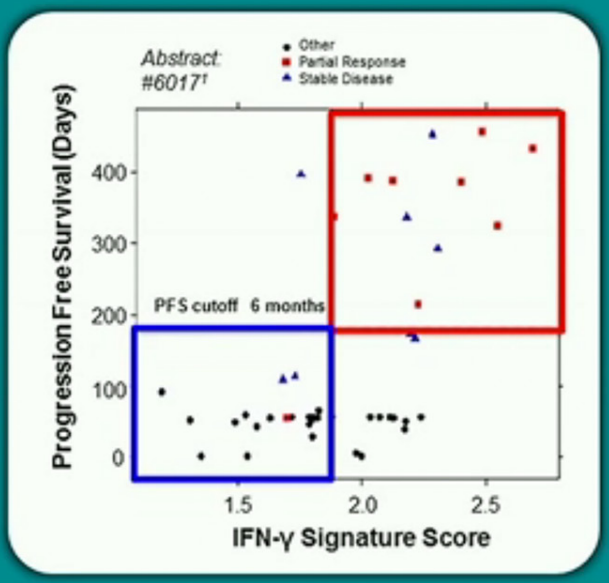
### Treatment Exposure and Response Duration of Patients Who Responded



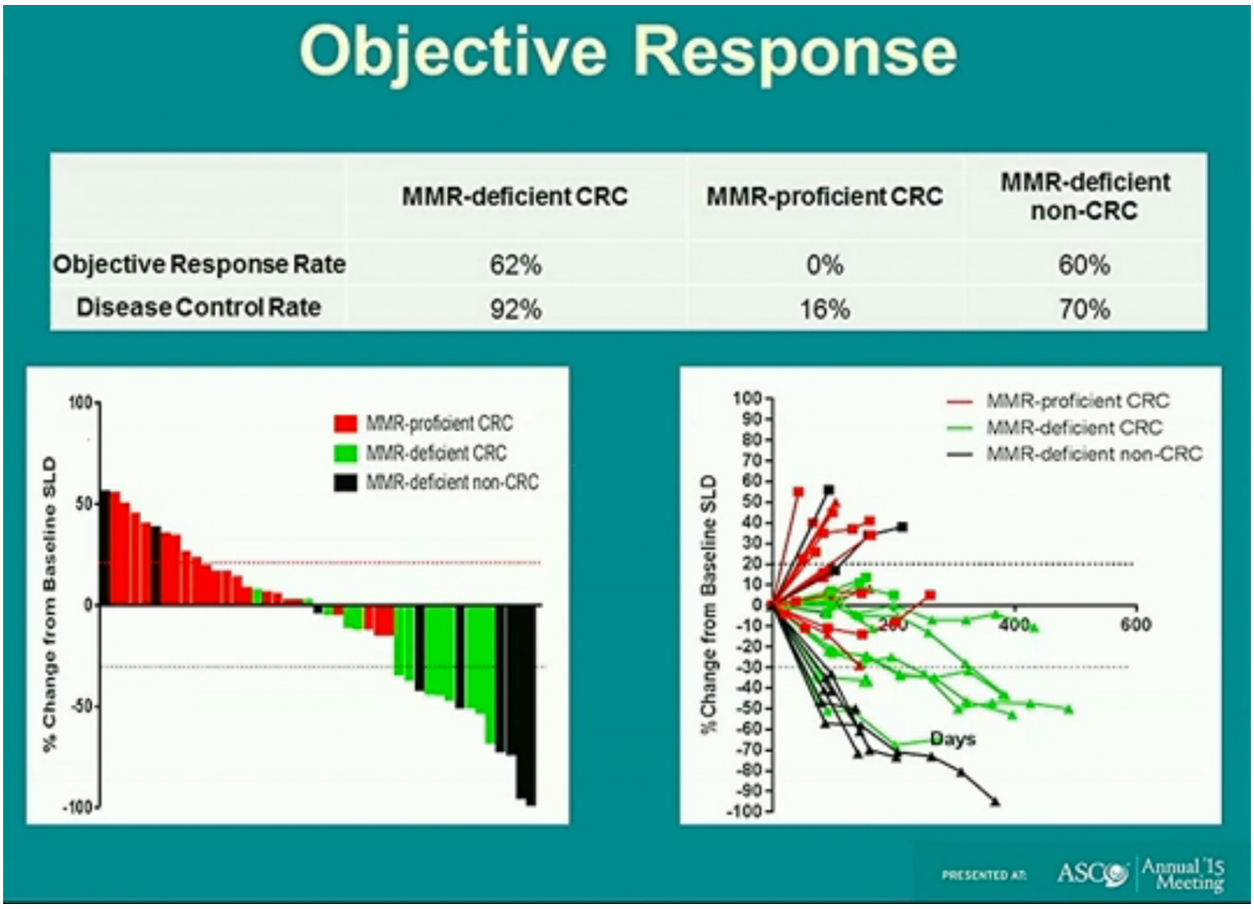

- Median follow-up duration:
  –5.7 (0.2 – 8.7) months
- Median time to response:
  –9.0 (7.6–18.0) weeks
- 40 patients remain on therapy
- **86% (25/29) of responding patients remain in response**

### Can We Predict Who Will Benefit? Potentially Yes…

- Evaluation of PD-L1 expression by IHC in the current cohort (B2) is ongoing
- The optimal cutoff for PD-L1 expression as well as potential clinical usefulness of PD-L1 as a clinical diagnostic for HNC remain to be determined
- An *Interferon-gamma* expression signature (abstract #6017) showed promise:[1]
  - 95% negative predictive value
  - 40% positive predictive value



## Mismatch Repair Deficiency Predicts Response to Keytruda




In the study, 132 patients with recurrent or metastatic squamous cell carcinoma of the head and neck received a fixed dose of Keytruda of 200 mg given as an infusion every three weeks. Of these patients, 59 percent had received two or more lines of prior therapy. Patients were not selected for this study based on PD-L1 status (a candidate biomarker that predicts response to PD-1/PD-L1 immunotherapy, such as Keytruda).

The majority (57 percent) of patients experienced some decrease in tumor size. The overall objective response rate was 24.8 percent (26.3 percent in HPV-negative patients and 20.6 percent in HPV-positive patients).

Keytruda was well tolerated, with serious side effects occurring in less than 10 percent of patients. The most common side effects were fatigue, rash, and itching; more serious immune-related side effects such as inflammation of lungs and colon were observed in a small number of patients.

Two phase III studies currently are evaluating Keytruda versus standard treatment in patients with recurrent/metastatic head and neck cancer.

**Mismatch Repair Deficiency Predicts Response to Keytruda**

A phase II study identified the first genomic marker—mismatch repair deficiency—to predict response to the anti-PD-1 antibody Keytruda. This marker predicted responses across a range of cancers.

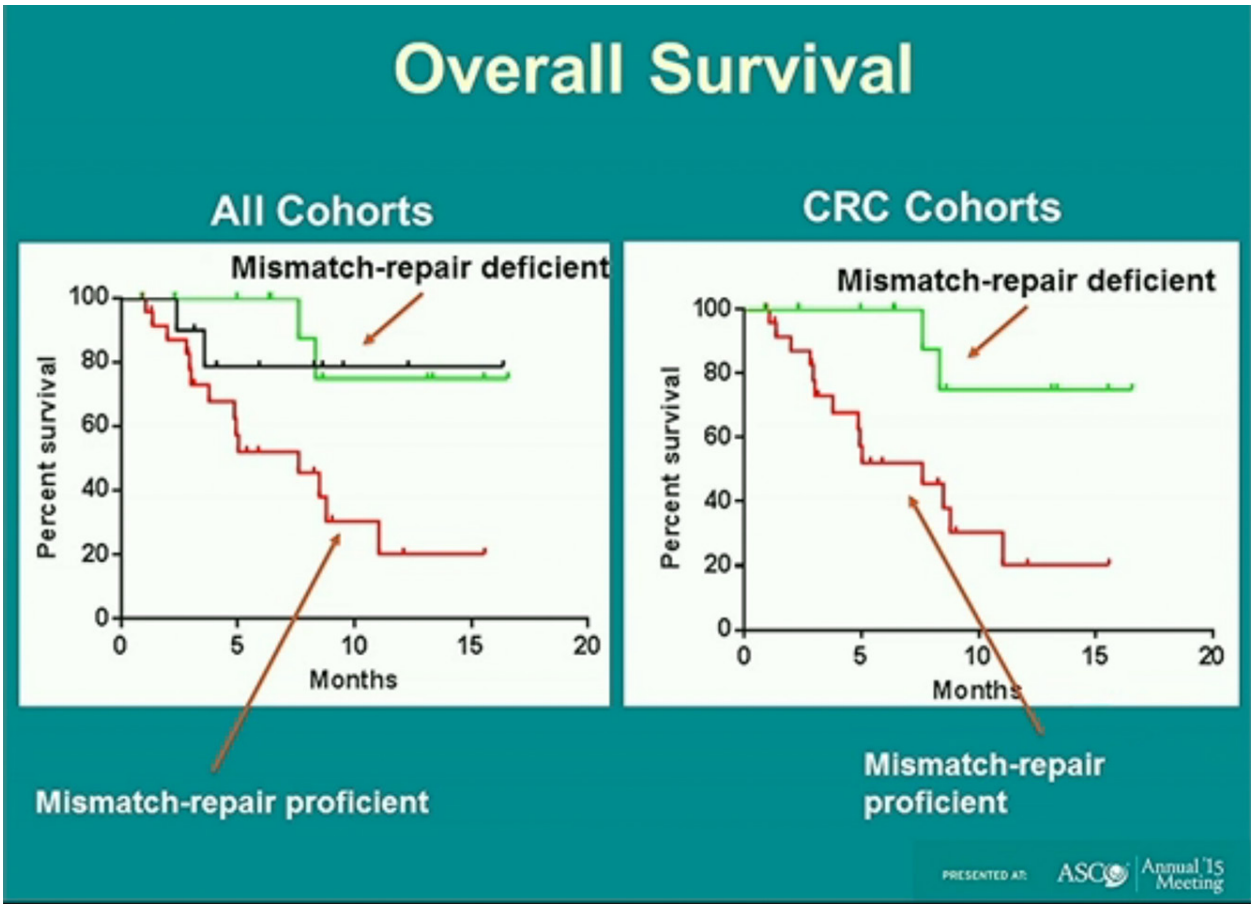
Among patients with colorectal cancer, 62 percent of those with MMR-deficient tumors experienced tumor shrinkage, while no responses were detected among those without this abnormality ("MMR-proficient"). The response rate among patients with other MMR-deficient cancers was similar—60 percent.

MMR deficiency is found in 15-20 percent of sporadic (non-inherited) CRCs and in nearly all CRCs associated with Lynch syndrome, which constitutes up to 5 percent of all CRCs. MMR deficiency is also found in other tumor types including stomach, small bowel, endometrial, prostate, and ovarian cancer.

Testing for MMR-deficiency is widely available and may enable doctors to identify a larger population of patients who might benefit from Keytruda and other PD-1 drugs.

"This study is really about bridging

## Mismatch Repair Deficiency Predicts Response to Keytruda




immunotherapy and genomics for the benefit of patients, and it has implications for a broad range of cancers," said lead study author Dung Le, an assistant professor of oncology at Johns Hopkins Kimmel Cancer Center.

MMR deficiency leads to an accumulation of genetic mutations in a tumor.

"When you have a tumor that has thousands of mutations, this increases the probability that the immune system can recognize and destroy the tumor," Le said. "So, we suspected that immune checkpoint inhibitors such as Keytruda would work particularly well against MMR-deficient tumors."

In this study, MMR-deficient tumors had an average of 1,782 mutations, compared to 73 mutations in MMR-proficient tumors. Higher numbers of mutations were linked to better response to Keytruda.

The study included three groups of patients: MMR-proficient metastatic CRC (25 patients), MMR-deficient metastatic CRC (13 patients), and other MMR-deficient cancers (10 patients). All patients had progressive metastatic cancer that had worsened despite prior treatment.

While researchers observed a large difference in response rates between MMR-deficient and -proficient CRCs (62 vs. 0 percent), the difference in disease control rates (tumor shrinkage or suppressed growth) was even greater—92 percent in the MMR-deficient group and only 16 percent in the MMR-proficient group. Blood marker changes such as CEA levels indicating response were seen within the first few weeks of starting treatment, and patients tended to feel better almost immediately.

In the group of other MMR-deficient cancers (excluding CRCs), the overall response rate was 60 percent. Responses were detected in patients with advanced endometrial cancer and several types of advanced gastrointestinal cancers including ampullary, duodenal, cholangiocarcinoma, and gastric cancers. Few treatment options exist for such patients. At last analysis, responses were ongoing for all but one patient, and many responses have lasted for over a year.

Le said the next step is to reproduce the findings of this prospective study in a larger group of patients to solidify the observation that MMR deficiency is a predictor of response to therapies targeting PD-1. She

noted that the durability of response with little toxicity could eventually lead to testing this approach in initial treatment for these patients.

**Opdivo-Yervoy Combination in Melanoma**

A randomized phase III trial indicates that initial therapy with Opdivo alone or in combination with Yervoy is significantly more effective than Yervoy alone for melanoma.

Opdivo alone more than doubled the average time to disease progression, compared to Yervoy (6.9 months vs. 2.9 months), and the benefit was even greater when the therapies were combined (11.5 months). The response rates were also substantially higher in patients receiving the combination therapy (57.6 percent) and Opdivo (43.7 percent) alone, as compared to Yervoy (19 percent).

"We're very encouraged that the initial observations about the efficacy of this combination held up in this large phase III trial," said lead study author Jedd Wolchok, chief of Melanoma and Immunotherapeutics Service at Memorial Sloan Kettering Cancer Center. "Our study also suggests that patients with a specific tumor marker appear to benefit the most from the combination treatment, whereas other patients may do just as well with nivolumab (Opdivo) alone. This will help doctors provide important insight for patients on which treatment is right for them.

Opdivo and Yervoy are monoclonal antibodies that block two different immune checkpoints—PD-1 and CTLA-4, respectively.

This study randomly assigned 945 patients with previously untreated, advanced melanoma to receive Yervoy, Opdivo, or the combination of the two. After a follow-up period of at least nine months, the median progression-free survival was 2.9 months for Yervoy, 6.9 months for Opdivo, and 11.5 months for the combination. The differences between the combination and Yervoy groups, and Opdivo and Yervoy were statistically significant.

The response rates for the combination, Opdivo, and Yervoy groups were 57.6 percent, 43.7 percent, and 19 percent, respectively. The average reductions in tumor burden (depth of response) were 52 percent with the combination and 34 percent with Opdivo alone. In contrast, patients who received Yervoy alone experienced a 5 percent increase in tumor burden.

As expected, the rate of serious drug-related side effects was the highest in the combination group (55 percent), and 36 percent of patients in this group had to stop the therapy due to side effects. Prior studies have shown that many patients who stop immunotherapy early still continue to do well, Wolchok noted.

This prolonged benefit is explained by the fact that immunotherapy works by activating the immune system rather than targeting the tumor directly. It is not yet clear how long patients need to be treated to fully activate the immune system, and the minimal duration of therapy probably varies from patient to patient.

In this study, Opdivo alone seemed to be as effective against PD-L1-positive tumors as the combination of Opdivo and Yervoy. For patients with PD-L1-negative tumors, however, the combination treatment was significantly more beneficial than Opdivo alone.

## ESMO Scale Stratifies Magnitude Of Benefit of Cancer Drugs

The European Society for Medical Oncology May 30 published the ESMO Magnitude of Clinical Benefit Scale, a tool to assist oncology clinicians in evaluating the most effective anti-cancer medicines for their patients.

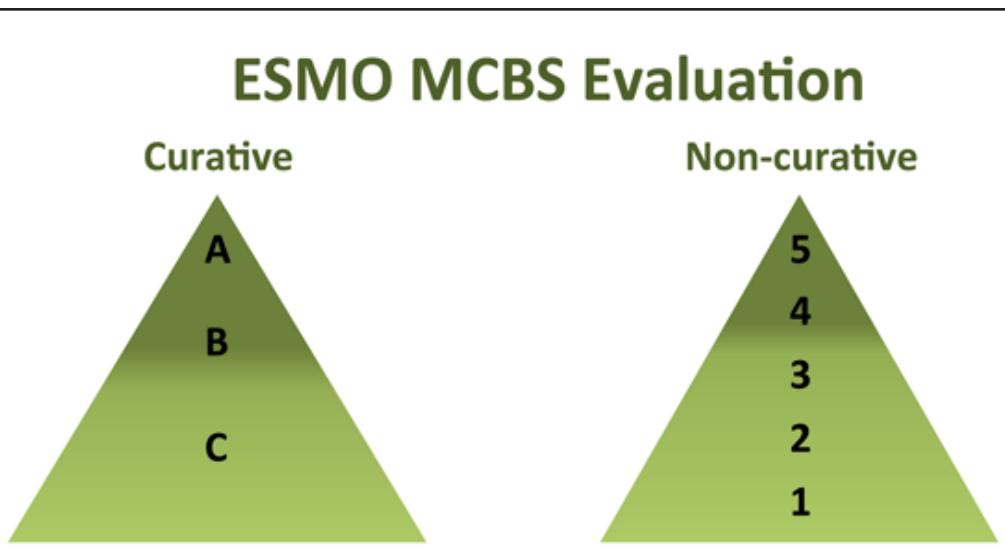
According to the society, the ESMO-MCBS offers a "rational, structured and consistent approach to stratify a drug's clinically meaningful benefit"—a scale that can be used in public policy decision-making, to develop or improve clinical guidelines, in day-to-day clinical situations.

A manuscript describing the project and reporting the main results from a field testing of the scale conducted on 77 cancer medicines across 10 cancer types was published May 30 in Annals of Oncology.

"While it is known that the value of any new treatment is determined by the magnitude of its clinical benefit against its cost, to date there has not been a standard tool for grading such magnitude," says Nathan Cherny, director of the Cancer Pain and Palliative Medicine Service, Department of Medical Oncology, Shaare Zedek Medical Center in Israel, who formulated the idea some years ago.

The ESMO-MCBS project was presented at the American Society of Clinical Oncology annual meeting in Chicago in an ASCO/ESMO joint session, called "Global Perspective on Value."

The session demonstrated how the scale could provide useful information when used in conjunction with the preliminary results of the European snapshot perception survey on anti-cancer medicine availability conducted last year.




**Curative - Evaluation form 1: for new approaches to adjuvant therapy or new potentially curative therapies**

**Non-curative - Evaluation forms 2a, b or c: for therapies that are not likely to be curative**

"As the international organization committed to the interest of the oncology community at large, we are concerned about some anti-cancer medicines approved by the European Medicines Agency not being available or affordable to patients when prescribed," ESMO President Rolf Stahel said. "With the ESMO-MCBS, we aim to signal the drugs with a large magnitude of clinical benefit which should be endorsed across Europe for rapid patient access, especially when these medicines are recommended through evidence-based standards set forth in the internationally recognized ESMO Clinical Practice Guidelines."

ESMO intends to apply the scale prospectively to new anti-cancer drugs that will be approved by the EMA. Drugs obtaining the highest scores on the scale will be highlighted in the ESMO Clinical Practice Guidelines, with the hope that they will be rapidly made available by health authorities across the European Union, ESMO said.

"In the absence of a standardized approach for grading the magnitude of clinical benefit, conclusions and recommendations derived from studies are often hotly disputed and very modest incremental advances have often been presented, discussed and promoted as major advances or 'breakthroughs,'" said Elisabeth de Vries, co-chair of the ESMO-MCBS Task Force, Department of Medical Oncology, University Medical Center Groningen, University of Groningen, The Netherlands.

"Application of the scale will reduce the likelihood that statements of clinical benefit will be distorted by either overestimation or overstatement on one extreme or nihilism at the other," de Vries said.

According to ESMO, the scale is presented in two parts in due consideration of the "profound" differences between the curative and palliative settings:

"As part of ESMO's ongoing work to integrate all aspects of oncology, we believe that a scale highlighting the most clinically effective new medicines plus a snapshot perception survey on the availability and affordability of existing medicines will provide useful insights for the oncology community to help move cancer treatment forward," said Alexandru Eniu, head of Day Hospital Unit, Cancer Institute Ion Chiricuta, Cluj-Napoca, Romania. Eniu is also ESMO Board member and chair of the ESMO Emerging Countries Committee, co-project leader of the ESMO European Consortium Study on the Availability of Anti-Neoplastic Medicines.

Richard Sullivan, Kings Health Partners Integrated Cancer Centre, King's College London, Institute of Cancer Policy, said: "The ESMO-MCBS is an important first step to the critical public policy issue of value in cancer care, helping to frame the appropriate use of limited public and personal resources to deliver cost effective and affordable cancer care."

# Canadian Judge Orders Tobacco Companies To Pay $12 Billion to About One Million Quebec Citizens

*By Nick Crispino*

A Quebec court ordered three major tobacco companies to pay US$12 billion, over 15 billion Canadian dollars, in damages in a landmark class action lawsuit.

On June 1, Quebec Superior Court Judge Brian Riordan instructed Canadian tobacco companies JTI-Macdonald, Imperial Tobacco, and Rothmans, Benson & Hedges to pay punitive and moral damages to two groups of Quebecois plaintiffs. The lawsuit was filed in fall 1998, and legal proceedings began in 2012.

Riordan condemned the firms' operations:

"The companies earned billions of dollars at the expense of the lungs, the throats, and the general well-being of their customers," Riordan said. "If the companies are allowed to walk away unscathed now, what would be the message to other industries that today or tomorrow find themselves in a similar moral conflict?"

The case marked the first time tobacco companies had gone to trial in a civil lawsuit in Canada. One group of plaintiffs—the Blais File—said that they became seriously ill from smoking. The second, the Létourneau File, claimed they became dependent on nicotine.

Riordan upheld the plaintiffs' claims that the companies committed four separate wrongdoings:

• Failing to properly warn their customers about the dangers of smoking,

• Underestimating of evidence relating to the harmful effects of tobacco,

• Engaging in unscrupulous marketing, and

• Destroying documents.

The Blais plaintiffs were given 90 percent of the $12 billion due to the severity of their claims. Those with cancer who began smoking before Jan. 1, 1976, will receive $80,000 while those who began smoking after that date will collect about $70,000. Plaintiffs with emphysema will receive $30,000 if they began smoking before January 1976, and $24,000 if they started smoking after.

The Létourneau group includes nearly one million people, which grants them a little over $100 a person.

All three companies will appeal, but Riordan ordered each to pay an initial compensation of over $800,000 within the next 60 days.

The companies expressed their dissatisfaction on the court's decision.

"Today's judgment ignores the reality that both adult consumers and governments have known about the risks associated with smoking for decades, and seeks to relieve adult consumers of any responsibility for their actions," said Tamara Gitto, vice president of law, and general counsel with Imperial Tobacco Canada. "We believe there are strong grounds for appeal and we will continue to defend our rights as a legal company."

JTI-Macdonald said Canadians have a "very high awareness" of the dangers when it comes to smoking, and that the evidence against the companies does not deserve such a conclusion.

"It's one more bit of evidence against an outlaw industry who are killing people all over the world and imposing gigantic social costs," said Stanton Glantz, the American Legacy Foundation Distinguished Professor of Tobacco Control at the University of California San Francisco. "Despite years of litigation and the mass amount of lawyers they have, a judge basically said the world is not flat.

"Other providences could be coming in and taking legal actions as well."

For plaintiff Lise Blais—whose husband filed one of the lawsuits and died from lung cancer in 2012—it can be seen as a bittersweet victory.

"Seventeen years is long, but I had my hope that we were going to win—and we did," Blais said in a statement.

**Ranking $12 Billion**

The sum of $12 billion is a very reasonable number, said Richard Daynard, president of the Public Health Advocacy Institute, and university distinguished professor of law at Northeastern University.

"The closest comparison is the Engle litigation in Florida," Daynard said to The Cancer Letter. "A subset of the cases—those in federal courts—were recently settled for over $100,000 per case.

"It's generally thought that the cases in state court, which have not yet been settled, will be worth somewhat more."

In March, tobacco giant R.J. Reynolds was ordered to pay $16.9 million in punitive damages—down from the original $23 billion pre-appeal—to Cynthia Robinson.

Her late husband, Michael Johnson Sr., was involved a class action suit filed by Howard Engle in

1994 against R.J. Reynolds and the Liggett Group, on behalf of a group of Florida citizens who suffered from smoking-related illnesses.

The Miami-Dade Circuit Court initially ordered the companies to pay $145 billion in punitive damages. In 2006, the Florida Supreme Court agreed with an appellate court to reverse the verdict, but allowed members of the original suit to file cases individually.

The largest known class action suit against tobacco companies was the 1998 Master Settlement Agreement—a $206 billion deal that resolved litigation brought by 46 states, the District of Columbia and five U.S. territories against four major U.S. cigarette manufacturers and industry trade associations.

Philip Morris, R.J. Reynolds, Brown & Williamson and Lorillard agreed to pay a minimum of $206 billion over 25 years for marketing and promotion of tobacco products.

The settlement also created and funded the National Public Education Foundation—dedicated to limiting youth smoking and researching diseases associated with smoking.

The MSA also created new restrictions, which prohibited tobacco advertising targeting people younger than 18, and eliminated cartoons in cigarette advertising as well as outdoor, billboard and public transit advertising.

About 40 tobacco companies signed the MSA and are bound by its terms.

## ASCO CEO Allen Lichter To Step Down In June 2016

(Continued from page 1)

On Lichter's watch, ASCO's total revenues grew from about $71 million in fiscal 2006 to $93 million in fiscal 2013, the most recent year for which data are publicly available.

The ASCO board of directors has selected a search advisory committee, led by ASCO President Julie Vose.

"ASCO expects the search to begin in September, which will give the committee plenty of time to find the very best candidate to lead the organization," ASCO officials said in a statement to The Cancer Letter.

Prior to becoming ASCO CEO, Lichter held two leadership roles at the University of Michigan—he was chair and professor of Radiation Oncology from 1984 to 1998 and dean of the medical school from 1998 to 2006.

At the University of Michigan, Lichter was the first Isadore Lampe Professor of Radiation Oncology, an endowed chair, and was the Newman Family Professor of Radiation Oncology. He previously served as the director of the Radiation Therapy Section of the NCI Radiation Oncology Branch.

Lichter's research and development of three-dimensional treatment planning led to a Gold Medal from the American Society for Radiation Oncology.

In 2002, Lichter was elected to the Institute of Medicine of the National Academies of Science. He has been a member of ASCO since 1980 and has served the society in various volunteer capacities.

*ASCO Annual Meeting*

## ASCO President Peter Paul Yu's 2015 Presidential Address

*An edited text of Yu's address follows:*

The shift to a value-based healthcare system, the advent of precision medicine, and the transition to digital health are forces driving unprecedented change in oncology. These are changes that will transform medicine within the professional lives of most everyone in this hall today. Ladies and gentlemen, how we respond to these changes will determine not only the future of our profession, but the health, comfort and care of millions of people around the globe.

Buenos Dias! Good morning! Da jia hao!

It is my great pleasure as president of the American Society of Clinical Oncology to extend the warmest of greetings to all of our members and distinguished guests. I thank Dr. [Allen] Lichter for that very kind introduction, and I join my colleague Charles Penley, chair of the Conquer Cancer Foundation, in welcoming you to the Opening Session of ASCO's Annual Meeting.

The theme of this year's meeting—transforming data into learning—is about how we use the tsunami of data generated by both precision medicine and clinical medicine to learn how to care for patients with cancer in the most compassionate, effective and sustainable manner—learning together from every patient's experience. ASCO is leading the move to a new data-driven era of discovery in clinical oncology.

Three critical steps are needed to transform molecular and clinical data into genuine learning:

- We must be able to assess outcomes that reflect the patient perspective.
- We have to innovate how we generate and

test new hypotheses in order to accommodate the accelerated pace of precision medicine.

• We need to learn how to apply the results of clinical trials to real world patients and real world realities of healthcare delivery.

These three steps define the true value of what we do. They are the tools that transform data into knowledge and knowledge into learning. If we do not define, measure and report the value of what we bring to patients, we will not be valued by society in turn.

Our keynote speaker, Michael Porter, has spoken to us about how patient-centered outcome measurements drive improvements in the patient experience and increase the value of healthcare. He reminds us that the true goal is not better or cheaper healthcare delivery, but better health.

At this year's meeting we will hear presentations about reducing short and long-term toxicities of cancer treatment, from mitigating chemotherapy induced hair loss to managing the health problems of long-term survivors of childhood malignancies.

We need and will do more to improve palliative care and survivorship for patients with cancer. ASCO's inaugural Palliative Care Symposium last October was highly successful and I expect that our inaugural Survivorship Symposium in 2016 will be equally so.

**Building on Precision Medicine**

For patients with cancer, the path to better health is dependent on studying the systems biology of cancer. At this session one year ago, Lee Hood shared with us his vision of the potential for precision medicine to generate enormous data sets that enable us to create new models—models that lead to more effective therapies with fewer side effects. But for now, we face a deluge of data steadily increasing in volume, velocity and variety that underscores the importance of collecting data so that it is readily accessible, searchable and usable.

International efforts are underway to amass large precision medicine data sets. Building on the Cancer Genome Atlas, the International Cancer Genome Consortium has been acquiring 25,000 patient biospecimens from 50 types of cancer to analyze germ line and somatic alterations in genome, epigenome and the transcriptome. In the United Kingdom, the 100,000 Genome Project has been launched.

We are well on the path towards building ever larger and more complex precision medicine data sets. We must also foster sharing of these data sets and the creation and adoption of technical standards to do so.

But patients are more than the digitalized representation of molecular data. alongside precision medicine is personalized medicine, the aspect of cancer care that speaks to patient preferences and behavior, the role of the environment and clinical interventions. It is just as critical to have useful clinical data sets such as aggregated medical records as it is to have large molecular data sets. Both are necessary to advance discovery and improve care.

The Global Alliance for Genomics and Health is an umbrella organization of 250 members, including ASCO, who believe that human health will be advanced faster through the sharing of genomic and clinical data sets. New international technical standards will enhance interoperability of data sets and allow genotype-phenotype correlations to be modeled and tested.

For example, the BRCA Challenge will accelerate our understanding of BRCA variants of uncertain significance by allowing investigators to share clinical outcomes data. CancerLinQ is ASCO's revolutionary health information technology that aggregates the electronic medical records of patients with cancer to create a shared clinical dataset. CancerLinQ is one example of how the daily work of individual oncologists can be leveraged for the greater good of all.

As precision medicine begins to bear fruit, we can expect that more investigational drugs will be fast tracked by FDA pathways such as break-through designations and regulatory approval based on phase I and II trials with exceptionally strong signals of efficacy. At this meeting we will hear about the first reports of several agents that have received break-through designation.

**Learning from Data**

We must continue innovation that accelerates the speed at which we transform data into learning. The research infrastructure constructed over the past 50 years lacks the capacity and agility to allow us to bring new treatment advances to patients at the scale now required. To succeed we need to re-engineer how we bring concepts to clinical trial, and design clinical trials that achieve more clinically meaningful advances. A faster, more nimble approach to learning is needed.

This year ASCO issued a formal policy statement calling on the oncology community to readdress widely held assumptions about phase I studies. As shown here, the clinical benefit of phase I study drugs in the era of targeted treatments can be equivalent to standard treatment options, with no worse toxicity.

In the past, phase I studies have been viewed as

toxicity defining studies with no therapeutic benefit. This view has been a deterrent to physician referral of patients and led to denial of insurance coverage. In this new era of targeted therapies, such a view is as anachronistic as hand-copied manuscripts.

ASCO has developed a model to facilitate the off label use of targeted agents while collecting a minimal dataset on safety and efficacy. Designed to study small cohorts of patients with matches of drug-to-biomarker as determined by an ASCO molecular tumor board, strong early signals of efficacy will inform the design of phase II studies.

Physicians and patients will benefit from a mechanism to gain access to targeted agents and the life sciences industry will benefit by finding more promising lines of investigation. ASCO Chief Medical Officer Richard Schilsky is leading the development of this study, known as the Targeted Agent and Profiling Utilization Registry, or TAPUR study, in which pharmaceutical companies will donate their drugs. This will be ASCO's first IRB-approved clinical trial.

Thus far this morning we have heard of the need to measure outcomes across the full cycle of care, reflecting a patient-centered perspective. We have discussed sharing of large data sets of both precision medicine and clinical data, and driving innovation in knowledge generation. Finally, we come to learning how to apply knowledge in the real world of patient care, whether that is the global health of low- and medium-resourced countries or value-based medicine in the United States.

The Institute of Medicine has championed the model of a Rapid Learning Health System that enables us to transform data into learning at a vastly accelerated pace by learning from the real world experiences of patients. It is based on a healthcare system that learns from itself by continuous measurement, assessment and improvement. Sharing of data and learning across healthcare providers are at the heart of Rapid Learning Health Systems. ASCO understands that a system that uses informatics to bring together clinicians across healthcare delivery will drive care innovation and implementation science.

**ASCO's CancerLinQ: A Powerful Tool**

Here again, I am proud to say that ASCO is out in front, leading. Since January, ASCO and SAP have combined our resources for the co-innovation of CancerLinQ, the world's first rapid learning health system for oncology. The SAP HANA system is an in-memory data management system whose data architecture and data mining tools are the reasons why SAP is the leading enterprise data company in so many industries. HANA is the digital health platform that will underlie CancerLinQ.

ASCO brings our deep knowledge of clinical oncology and SAP brings the superior engineering prowess and project management needed to bring a new product to market. The great strength of the collaboration however, is our mutual commitment and excitement to explore together that which yet needs to be discovered in this new frontier.

Fifteen pioneering community practices, hospital systems and cancer centers, with great vision and dedication, will provide CancerLinQ with the entire electronic health record data of their patients; they are our vanguard practices. By year-end digital health data from these practices will begin to flow through the CancerLinQ platform, bringing it to life. We have prepared this brief video on CancerLinQ and invite you to see the entire presentation in the Exhibit Hall.

With CancerLinQ we have a powerful tool to study and learn from all patients, whether on clinical trials or through clinical practice. This is a transformational change that addresses a need shared by all countries and all patients with cancer. There are many ASCO programs that can be adapted to support education and quality improvement throughout the world. With international oncologists now comprising one third of our membership, ASCO must reach out across the world to learn how we can help our members improve the state of cancer care.

In March, I travelled to South America. At the Durand Hospital in Buenos Aires, I met dedicated ASCO members who strive to provide the best patient care while working with limited resources and who self-impose an expectation that every oncologist will publish two papers each year.

In Uruguay, their NCI is building an informatics infrastructure that will link electronic health records and registries, create clinical decision support tools and establish a national bioinformatics testing and biobank facility.

Traveling to Brazil, I visited a 25-physician oncology clinic that is proud of its QOPI participation. Sao Paolo impresses with the extraordinary oncology care provided in private hospitals such as the Syrian-Lebanese and public hospitals such as ICSEP. In one public hospital dedicated to the treatment of women with cancer, I found this poster displayed at the front of a crowded patient waiting area. In Portuguese, it explains to patients the workflow for breast lesions, from imaging

to biopsy, surgery, radiation and medical oncology. At the bottom, the figure describes a 41 percent reduction in patients presenting with advanced disease and a 20 percent reduction in mortality, achieved through patient engagement in their own healthcare.

Everywhere, the dedication of ASCO members to their patients and their profession, their thirst for knowledge and their dedication to applying that knowledge with the limited resources available is palpable. Over and over, each country demonstrated the desire to achieve the highest standards and a trust in ASCO to assist them in their endeavors. It is a trust that we must uphold.

**Upcoming ASCO Programs**

This year's Annual Meeting launches the Society's Global Oncology Symposium. Each year, the symposium will highlight a high impact cancer that may have unique or common characteristics from country to country; this year it is gastric cancer. Solutions or models that address healthcare delivery challenges, such as provision of pathology services in low- and medium-resourced countries will be presented. With much of the world's cancer community present at the Annual Meeting, the symposium provides the ideal international meeting venue for discussing global oncology.

Later this year, ASCO will launch publication of the online Journal of Global Oncology which is the only journal dedicated to publishing original research related to cancer in low- and medium-resourced nations. The intent of the Journal of Global Oncology is to foster international collaboration among researchers, while providing mentorship to authors that will ensure that the highest editorial standards are achieved. We are fortunate to have Dr. David Kerr, a leader in global health from Oxford University, as the founding editor of this journal.

This is only a start. A presidential task force led by past ASCO president Gabriel Hortobagyi has been charged by the ASCO Board of Directors to study and advise on how our society can contribute to improving oncology global health by supporting our members as they engage the oncology ecosystem of education, research, industry and regulatory policy.

Ultimately, the need for an affordable, sustainable healthcare system is universal. Every nation on earth, regardless of how its physicians are trained, deployed and reimbursed, is faced with the need to provide the best possible care within the financial constraints of their system. Here in the United States, this is being defined by value-based medicine and provider payment reform.

The move away from fee-for service reimbursement to bundled payment models has begun. Secretary of Health & Human Services Sylvia Burwell has announced that by 2018, 50 percent of Medicare payments to physicians will be though alternative payment models. The Oncology Care Model from the Medicare Innovation Center brings together federal and private payers in a five-year pilot project of episodes of payment for chemotherapy services.

And the recently enacted bill repealing the Sustainable Growth Rate formula sets in motion a series of payment reforms such as the Merit-Based Incentive Payment System, or MIPS, that will consolidate and expand the current array of performance programs, and set incentives and penalties that may be as high as twenty-nine percent of total Medicare physician reimbursement.

These payment reform efforts seek to achieve the triple aim of the Institute of Healthcare Improvement, which are to improve the patient experience, improve population health and reduce the cost of care. This will necessitate improved patient access to care, coordination of care through oncology medical homes and discussions with patients on cost of care and end-of-life care.

Value of care cannot be assessed without measurement of the quality of care received. ASCO's quality improvement program, QOPI, will be a key part of implementing any payment reform model. One of those models is ASCO's Patient Centered Oncology Payment which bases reimbursement on flexible monthly bundles that reflect the acuity and complexity of the patient's needs, a greatly simplified billing schedule and a model that is not tied to the current fee schedule that drives physician encounter-based payment.

The last decade has been painful for community oncologists, who have suffered practice closures, mergers and decreased incomes. We have witnessed disruptions to patient care in the setting that delivers the majority of cancer care in the United States. If community oncology is to survive, we must together find our way forward by designing and embracing new payment models that reward the achievement of patient-centered outcomes and value the work of the healthcare providers who care for patients with cancer.

A part of improving the value of care is raising our expectations of clinical trial results that are considered meaningful advances in patient care. With our Clinically Meaningful Outcomes Statement, ASCO has initiated that discussion. Four sets of experts evaluated current standards of care in the first line therapy of advanced pancreatic cancer, triple negative

breast cancer and non-small cell lung cancer, and the treatment of colon cancer refractory to standard care.

Their goal was to determine the minimal improvement in overall survival that would constitute a clinically meaningful advance over current standard of care treatment. Working independently they concluded that a clinically meaningful advance should demonstrate a HR of at least 0.8, which translates into an improvement in median overall survival of two-and-a-half to six months depending on clinical context.

ASCO's Value Framework, scheduled to be published in the Journal of Clinical Oncology in late June, is designed to support physician and patient discussions of the clinical benefit, clinical toxicity, and financial cost of therapies that have been compared in randomized clinical trials. Patients need to have accurate information about expected benefit, toxicity and cost as well as a context for comparing new and typically more expensive, treatments to standard alternatives. With this understanding, they are better equipped to make a choice that is consistent with their personal goals, preferences—and finances.

At price points of $20,000 a month for new drugs, these discussions cannot be avoided any more, uncomfortable and unfamiliar as we may be with them. Ultimately, decisions will be made between patients and their healthcare providers. Collectively, these decisions will drive the level of demand for new diagnostics and therapeutics, which in turn may help influence more rational pricing of these products.

One of the greatest values that ASCO brings is in the nurturing of the next generation of oncologists. Since 1984, ASCO has helped launch almost 1,000 careers through our Young Investigator Awards to oncology fellows whose interests vary from translational bench research to research into improving the patient experience. This is the seed funding that provides tangible support for the innovation and energy that ensures our future. Fifty-eight YIAs, a record number, have been awarded this year, but even more would have been funded had we the resources to do so.

At this meeting, the Conquer Cancer Foundation launches a $150 million dollar campaign and over one third of the dollars donated will go to support groundbreaking research being done by both young investigators as well as more seasoned researchers I urge you to contribute generously so that the Conquer Cancer Foundation can support oncologists who make a difference by thinking creatively.



**Thank You**

Over the last five years, it has been my privilege to serve on the ASCO Board of Directors and have the opportunity to take a longer and broader perspective, to look back and see the incredible progress we have made over the course of 50 years, and to look forward to the future ahead.

The task has been made easier and all the more rewarding working with our chief executive officer Dr. Allen Lichter and the ASCO staff whose dedication to serve is equal to any of us here today and who help make ASCO the preeminent scientific and educational organization in the oncology community. Truly, it has been an honor for me to serve as the president of ASCO during this past year, and I would like to especially thank my Scientific Program Committee Chair, Dr. Alan Venook and my Education Committee Chair, Dr. John Cox who together have led the planning of this meeting. It has been my great fortune to have had three outstanding leaders in oncology as mentors through my career and I owe a great debt to Drs. James Holland, Larry Norton, and John Mendelsohn.

A mere 50 years after the founding of the American Society of Clinical Oncology, the confluence of precision medicine, rapid learning, and digital health prepares us for a similar incunabulum in medicine. Illumination and innovation—the transformation of data into learning—evokes nothing less. Is it the relationship between the humanistic side and the biologic determinants of our lives? Do all the answers to cancer lie in precision medicine and molecular testing? Is the art of medicine fading away?

Ladies and gentlemen, honored guests: it is our responsibility to confront the challenges before us. But bearing witness to the past 50 years of progress and the drivers of disruptive change that can be wind in our sails, it is a responsibility that we are proud to accept.

The first 50 years of clinical oncology saw a transformation in our understanding and treatment of the disease. Fifty years ago, cancer was not only incurable; it was a diagnosis that left patients to endure physical suffering compounded by social disgrace and ostracism. It was the sore that did not heal.

Today, as oncologists, we stand at the end of that beginning. In the next 50 years, we will work together to create an incunabulum—a period of knowledge and learning for the benefit of patients with cancer so that more patients, most patients, maybe all patients, will be cured. We owe it to patients past and present—and most of all to generations of patients yet to come—to do no less.

Thank you.

## Amgen Seeks to Depose Reporter, TCL Invokes First Amendment Shield

Amgen Inc. is seeking to depose The Cancer Letter editor and publisher Paul Goldberg in connection with a shareholders suit stemming from his 2007 story about the results of a Danish trial of Aranesp.

The Cancer Letter is contesting the subpoena, asserting first amendment protection and its rights to protect confidentiality of sources.

The story showed that the trial in question—one of Amgen's "pharmacovigilance trials" intended to determine whether the agent was safe at higher targets—was halted because of significantly inferior outcomes from adding Aranesp to radiation therapy.

A story about Amgen's efforts to subpoena Goldberg was published on The Wall Street Journal's Pharmalot blog June 5.

Amgen seeks to ascertain how The Cancer Letter learned about the Danish study and how this information was distributed (The Cancer Letter, Feb. 16, 2007). The company previously sought production of records late last year, and The Cancer Letter has filed an opposition to that effort.

The story about the Danish trial led FDA to intensify its scrutiny of these overprescribed products by issuing a clinical alert and scheduling a meeting of the FDA Oncologic Drugs Advisory Committee.

On Feb. 16, 2007, The Cancer Letter reported that Amgen had known about the discontinuation of the Danish study, but didn't disclose this outcome publicly. After the story appeared, the company held a 4 p.m. conference call to state that as a matter of policy it doesn't disclose the results of investigator-initiated studies and that it was under no obligation to do so.

However, Kevin Sharer, then Amgen president, chairman and CEO, acknowledged that "in retrospect, it would have been ideal" to disclose the Danish result and pledged to disclose such events in the future (The Cancer Letter, Feb. 23, 2007).

The shareholders suit prompted by this incident went to the U.S. Supreme Court, which addressed a technical matter, clearing the way for the lawsuit to proceed.

The Cancer Letter has notified Amgen's attorneys that it intends to seek sanctions against the company if it continues to demand access to information this publication deems confidential.

A letter to Amgen's attorneys from Steven Lieberman, an attorney with the Washington law firm of Rothwell Figg, who represents The Cancer Letter, is posted here.

*Obituary*

## Wally Sampson, 85, Challenged Alternative Remedies

*By Nick Crispino*

Wallace Ira Sampson, a longtime "quackbuster," emeritus clinical professor of medicine at Stanford University, and former director of oncology at the Santa Clara Valley Medical Center, died May 25 following a three-month hospital stay for complications following cardiac surgery. He was 85.

Sampson was one of a group of scientists and physicians who focused on the growing influence of alternative medicine, said Stephen Barrett, a fellow quackbuster.

"Sampson was highly educated, well informed, and a skilled editor," Barrett said to The Cancer Letter. "He had a lot of original work and was the first person who sounded the alarm about the infiltration of alternative quackery in medical schools. When it came to technology, there have not been a lot of people who have the ability to look at the statistical reasoning within scientific papers and he's one of the few people who could do that effectively."

Barrett is a retired psychiatrist, author, co-founder of the National Council Against Health Fraud, and the webmaster of Quackwatch.

During the 1980s, Sampson chaired the California Cancer Advisory Council, which was a major force in combating cancer fraud in the state. He also served as board chairman of the National Council Against Health Fraud (1990-1998) and editor of the journal Scientific Review of Alternative Medicine.

Born and raised in Hollywood, Calif., the son of David James Sampson, a pelt wholesaler, and Bernice (née Freilich), Sampson spent most of his life in Los Altos, Calif.

Sampson attended UCLA as an undergraduate, and received his M.D. from UC Berkeley and UCSF. He met his wife Rita and her son Rob while he interned at Minneapolis General Hospital, where she worked as a nurse.

They married at Fort Sam Houston, Texas, right after he completed boot camp, and left for Frankfurt, Germany, where, a year later, his son Paul was born. After completing his military duty Sampson returned

with Rita and their two sons to Los Angeles, where Buck, Dan, and David were born.

"He raised five of us boys, and while none of us went into medicine, all of us chose disciplines that demand critical thinking and somewhat of a familiarity with science," said David Sampson, director of media relations at the American Cancer Society. "We credit him with turning us into the kind of adults who ask the same kinds of questions he always asked. We now know these critical thinking skills are really vital to society moving forward.

"My own interests in cancer and becoming a cancer journalist—and now PR person—was sparked by spending Saturdays in the medical library while he was making the rounds and meeting patients," David said to The Cancer Letter. "It's little things like that that make me remember him fondly. He was a really gentle soul, funny, cute and at the same time really challenged all of us to ask tough questions."

After completing his residency at Harbor General Hospital in Los Angeles, Sampson became a resident in hematology at UCSF and the family moved to Oakland, Calif. Shortly thereafter, Sampson began his career as a physician of internal medicine and oncology at the Sunnyvale Medical Clinic.

He went on to start a private practice adjacent to El Camino Hospital in Mt. View, Calif., eventually ending his medical career as the director of oncology at the Santa Clara Valley Medical Center. He was also an early advocate for the right of terminally ill patients to die in the comfort of their own homes.

"I first encountered Wally (as his friends called him) through his writings deconstructing various forms of quackery on websites like Quackwatch and warning how unscientific medicine was worming its way into medical academia," said David Gorski, a surgical oncologist at the Barbara Ann Karmanos Cancer Institute specializing in breast cancer surgery, where he also serves as the Medical Director of the Alexander J. Walt Comprehensive Breast Center and Cancer Liaison Physician for the American College of Surgeons Committee on Cancer.

"Indeed, his 2002 article on the National Center for Complementary and Alternative Medicine, now known as the National Center for Complementary and Integrative Health, was one of the earliest articles I read that convinced me that this sham of an abomination of a waste of taxpayer dollars must be defunded," Gorski said to The Cancer Letter. "It is a classic that applies today every bit as much as it did 12 years ago. It was something that I had a hard time believing at first, but his writings and warnings both alarmed and educated me. They were a major influence on my development as a skeptic.

"Wally Sampson was an inspiration whose efforts predated mine by decades. He made his name in the anti-quackery movement back in the 1970s, when I was a teenager. What's little known about him is that he was one of the earliest skeptics involved in showing that laetrile was ineffective, even testifying in front of the FDA, and he stated that there is no dichotomy between 'Eastern' and 'Western' medicine long before I ever started saying it."

In retirement, Sampson accepted a professorship and taught courses at Stanford University, and started the journal The Scientific Review of Alternative Medicine.

"He did countless interviews with television, radio, and print journalists as he fought tirelessly to maintain high levels of scrutiny and review for alternative medical practices and remedies," David said.

"In addition to the many patients whose lives were touched by his care, he also leaves a powerful legacy through his later work teaching journalists and the lay public to use evidence to form their viewpoint on unproven treatments, an approach once viewed as cynical, but now demanded of journalists reporting on health matters."

Harriet Hall, a retired Air Force physician and flight surgeon who writes about pseudoscientific and alternative medicine, said Sampson was responsible for launching her career.

"I never really got to know Wally that well, but he changed my life forever," Hall said to The Cancer Letter. "I didn't meet him until I was in my late fifties, when I attended the 2002 Skeptic's Toolbox. At the time, I knew next to nothing about alternative medicine or about how to critique a scientific study.

"As part of his presentation, Wally showed a video of the Scientific American Frontiers episode on chiropractic in which Alan Alda said that chiropractic neck manipulation was associated with a significant percentage of strokes. I questioned that, and when I got home I did my own research and determined that the claim was true.

"In the process, I stumbled upon a lot of other things about chiropractic that intrigued me enough to make me read everything I could find on it, both pro and con. One thing led to another. You might say chiropractic was my gateway drug to critiquing alternative medicine, and it might never have happened if Wally hadn't sparked my interest.

"I wish I could have gotten to know him better.

He was kind, gentle, grandfatherly, professorial, approachable, modest, and a true gentleman. My daughter attended the Toolbox with me when she was a teenager, and she was quite fond of Wally. When we chanced to see him being interviewed on television, she would say, 'Look, there's Grandpa Wally!'

"Wallace Sampson was my mentor. He was responsible for launching my writing career and for making me who I am today. He is gone, but his work in science and skepticism will never be forgotten. Thank you, Wally. Requiescat in pace."

Sampson is survived by his wife of 59 years, Rita (née Landry) Sampson, brother Sandy, sons Robert, Paul (Suzanne), Buck (Kathryn), Dan (Dolores), and David, and grandchildren Peter, Rachel, Julia, Annie, Lorenzo, Lila, Rebecca, Maya, and Rylan. No memorial service is planned at this time.

*Matthew Bin Han Ong contributed to this story.*

*In Brief*

## Robinson Named Fred Hutch VP of Industry Relations

**NICOLE ROBINSON** will lead the Industry Relations and Technology Transfer office at **Fred Hutchinson Cancer Research Center**. Robinson will begin her role as vice president of industry relations and business development on July 27.

Robinson comes from Cincinnati Children's Hospital Medical Center where she served as assistant vice president of the Center for Technology Commercialization, leading the technology transfer and commercialization development team. During her nine years at Cincinnati Children's, Robinson increased the medical center's invention disclosures tenfold while doubling the active commercial licenses executed, resulting in over $60 million in licensing revenue. Prior to that, she managed IP assets for the Office of Technology and Intellectual Property at the University of Chicago.

The Industry Relations and Technology Transfer Office is responsible for managing and commercializing the intellectual property assets of Fred Hutch. The activities of the office span the technology transfer process—including invention disclosure, market evaluation, intellectual property protection, licensing and contract management, and collaborations with industry and venture partners.

**THE DEPARTMENT OF DEFENSE appropriations bill** for the 2016 fiscal year includes an additional $12 million for lung cancer research under the Congressionally Directed Medical Research Program. The bill has been approved by the House Appropriations Committee.

This is an increase of nearly 15 percent over last year, bringing the total amount of federal funding secured to-date to $101.5 million, according to the Lung Cancer Alliance. The bill is expected to be considered by the House in the coming weeks.

"Another milestone has been reached for the lung cancer community, said Laurie Fenton Ambrose, president and CEO of LCA. "We remain grateful to our lawmakers for their continued support of and investment in this much needed pipeline as it is contributing to our knowledge and understanding of how to better prevent, detect and treat lung cancer."

Since its inception, the CDMRP has funded more than 110 lung cancer projects, supporting research into non-or minimally invasive detection and screening tools, mechanisms leading to various subtypes of lung cancer, the progression to clinically significant lung cancer, prevention and treatment, predictive and prognostic markers to identify responders, among others. In FY2013, CDMRP also funded the Lung Cancer Biospecimen Resource Network, an open access bio repository that provides specimens for scientific research by academic centers and private industry worldwide.

**THE COMMUNITY ONCOLOGY ALLIANCE** announced that nine practices received accreditation as oncology medical homes through a pilot program by the Commission on Cancer.

The commission bestowed full and contingent accreditation on the following community oncology practices: **Austin Cancer Center**, Austin, Texas; **Center for Cancer and Blood Disorders**, Ft. Worth, Texas; **Dayton Physicians Network**, Dayton, Ohio; **Hematology Oncology Associates of Central New York**, East Syracuse, N.Y.; **Maine Center for Cancer Medicine**, Portland, Maine; **New Mexico Oncology Hematology**, Albuquerque, N.M.; **Northwest Georgia Oncology Center**, Marietta, Ga.; **Oncology Hematology Care**, Cincinnati, Ohio; and **Space Coast Cancer Center**, Titusville, Fla.