SARAH CANNON
Research Institute

Innovative Solutions and Best Practices: Excellence in Cancer Clinical Research

Howard A. Burris, III, MD
ASCO President
Chief Medical Officer, Sarah Cannon

THE CHANGING LANDSCAPE: FROM WEEKLY PACLITAXEL TO PILLS AND CHECKPOINTS

- Drugs: Chemo to ADC's, TKI's, and IO
- Trials: Phase 1 to 3 is now FIM to POC
- Approach: "one size fits all" to "personalized driven by biology"

FDA ONCOLOGY APPROVALS

1998 FDA Approvals

8

2018 FDA Approvals

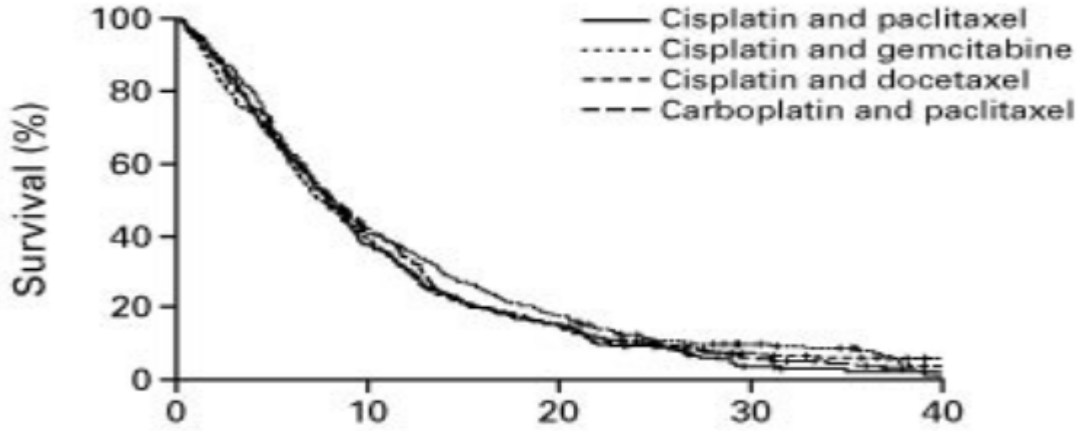
49

SARAH CANNON
Research Institute

ORIGINAL ARTICLE

Comparison of Four Chemotherapy Regimens for Advanced Non–Small-Cell Lung Cancer

Joan H. Schiller, M.D., David Harrington, Ph.D., Chandra P. Belani, M.D., Corey Langer, M.D., Alan Sandler, M.D., James Krook, M.D., Junming Zhu, Ph.D., and David H. Johnson, M.D. for the Eastern Cooperative Oncology Group



N = 1207

January 10, 2002
N Engl J Med 2002; 346:92-98
DOI: 10.1056/NEJMoa011954

SARAH CANNON
Research Institute

2018-2019 SINGLE ARM TRIAL HEMATOLOGY/ONCOLOGY APPROVALS (WWW.FDA.GOV)

- Pembrolizumab (KEYTRUDA, Merck & Co., Inc.) for patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy. N=83
- Ruxolitinib (JAKAFI, Incyte Corporation) for steroid-refractory acute graft-versus-host disease (GVHD) in adult and pediatric patients 12 years and older. N=49
- Ivosidenib (TIBSOVO, Agios Pharmaceuticals, Inc.) for newly-diagnosed acute myeloid leukemia (AML) with a susceptible IDH1 mutation, as detected by an FDA-approved test, in patients who are at least 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy. N=28
- Erdafitinib (BALVERSA, Janssen Pharmaceutical Companies) for patients with locally advanced or metastatic urothelial carcinoma, with susceptible FGFR3 or FGFR2 genetic alterations, that has progressed during or following platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy. N=87
- Tagraxofusp-erzs (ELZONRIS, Stemline Therapeutics), a CD123-directed cytotoxin, for blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older. N=13
- Calaspargase pegol-mknl (ASPARLAS, Servier Pharmaceuticals LLC), an asparagine specific enzyme, as a component of a multi-agent chemotherapeutic regimen for acute lymphoblastic leukemia (ALL) in pediatric and young adult patients age 1 month to 21 years. N=124
- Pembrolizumab (KEYTRUDA, Merck & Co., Inc.) for adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC). N=50
- Gilteritinib (XOSPATA, Astellas Pharma US Inc.) for treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with FLT3 mutation as detected by an FDA-approved list. N=138
- Larotrectinib (VITRAKVI, Loxo Oncology Inc. and Bayer) for adult and pediatric patients with solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation, that are either metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory alternative treatments or whose cancer has progressed following treatment. N=55
- Pembrolizumab (KEYTRUDA, Merck & Co., Inc.) for patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. N=104

CHALLENGES IN CLINICAL RESEARCH

- Vast numbers of trials
- Expansion cohorts
- Rare mutations
- Education
- Eligibility criteria
- Patient access
- Trial complexity
- Overwhelming paperwork
- Data (volume, interpretation)

INNOVATIVE SOLUTIONS: Genospace and Molecular Cancer Conferences

SARAH CANNON
Research Institute

NGS TESTING - IN THE NEWS

DRUG DISCOVERY & DEVELOPMENT

FDA Finalizes Guidances for Next-Generation Sequencing Tests

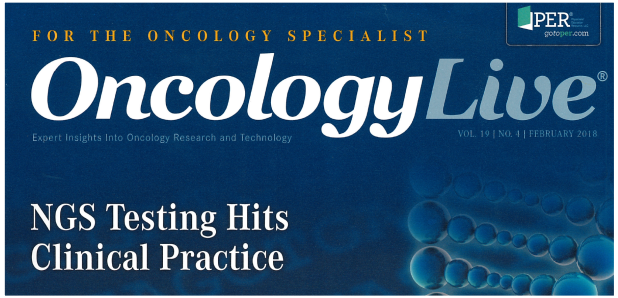
Fri, 04/13/2018 - 9:58am by FDA

JOURNAL OF CLINICAL PATHWAYS

Next-Generation Sequencing Proves Cost-Effective in Metastatic NSCLC

05/17/18

An economic model comparing different types of genetic testing in metastatic non-small cell lung cancer (NSCLC) showed that next-generation sequencing (NGS) is more cost-effective than testing for one or a limited number of genes at a given time.



HEALTHCARE FINANCE

MAR 16 | MORE ON ANALYTICS

CMS approves Next Generation Sequencing for cancer patients

The FoundationOne CDx test is the first breakthrough-designated in vitro diagnostic test and can detect genetic mutations in 324 genes.

Susan Morse, *Senior Editor*

The Centers for Medicare and Medicaid Services has finalized coverage of Next Generation Sequencing for cancer patients.

Targeted Oncology

Next-Generation Sequencing for Metastatic NSCLC Associated With Substantial Cost Savings

Angelica Welch
Published Online:5:05 PM, Wed May 16, 2018

Forbes

MAR 6, 2018 @ 10:30 AM 9,474

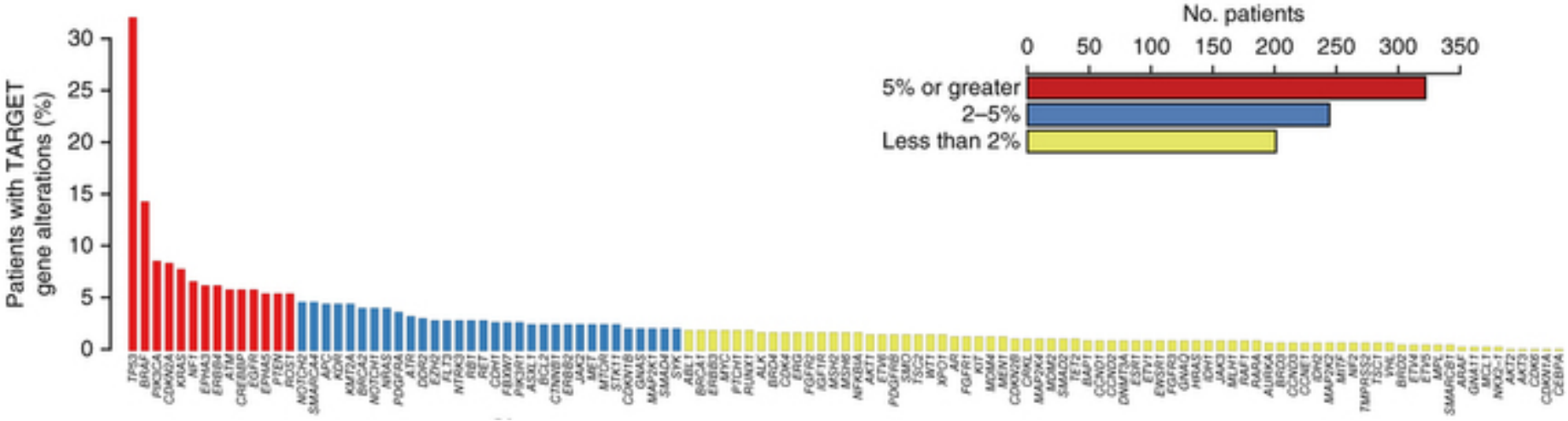
All Cancer Patients Should Have Access To Genomic Testing

Days after Thanksgiving, the FDA approved Foundation Medicine's comprehensive genetic test for evaluating cancer. The idea—and practice—of testing tumors for specific DNA or protein abnormalities is not new. Previously, the agency listed several dozen approved companion diagnostic tests; these earlier tools check one or a few molecules to inform the cancer subtype, prognosis, and likelihood of response to treatments.

WHY DO WE NEED TO PROFILE PATIENTS

- For the patient/individual benefit
- For clinical research/drug development (trial accrual)
- For cancer research/benefit of all (biology, resistance)

THE CHALLENGE OF PRECISION MEDICINE



Van Allen et al. Nature Medicine 2014;20:682-688

OPPORTUNITY

As new data and technologies emerge, clinicians are required to interpret and act upon increasingly complex information

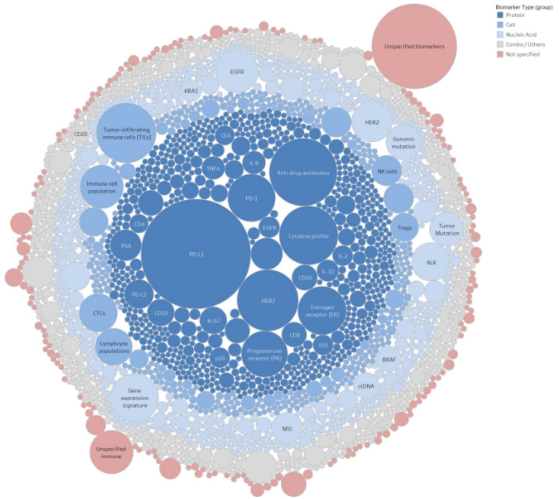
DNA Gene List: Entire Coding Sequence for the Detection of Base Substitutions, Insertion/Deletions, and Copy Number Alterations

ABL1	*ABL2*	*ACVR1B*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*AMER1 (FAM123B)*	*APC*	*AR*
ARAF	*ARFRP1*	*ARID1A*	*ARID1B*	*ARID2*	*ASXL1*	*ATM*	*ATR*	*ATRX*	*AURKA*
AURKB	*AXIN1*	*AXL*	*BAP1*	*BARD1*	*BCL2*	*BCL2L1*	*BCL2L2*	*BCL6*	*BCOR*
BCORL1	*BLM*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*BRIP1*	*BTG1*	*BTK*	*C11orf30 (EMSY)*
CARD11	*CBFB*	*CBL*	*CCND1*	*CCND2*	*CCND3*	*CCNE1*	*CD274*	*CD79A*	*CD79B*
CDC73	*CDH1*	*CDK12*	*CDK4*	*CDK6*	*CDK8*	*CDKN1A*	*CDKN1B*	*CDKN2A*	*CDKN2B*
CDKN2C	*CEBPA*	*CHD2*	*CHD4*	*CHEK1*	*CHEK2*	*CIC*	*CREBBP*	*CRKL*	*CRLF2*
CSF1R	*CTCF*	*CTNNA1*	*CTNNB1*	*CUL3*	*CYLD*	*DAXX*	*DDR2*	*DICER1*	*DNMT3A*
DOT1L	*EGFR*	*EP300*	*EPHA3*	*EPHA5*	*EPHA7*	*EPHB1*	*ERBB2*	*ERBB3*	*ERBB4*
ERG	*ERRFI1*	*ESR1*	*EZH2*	*FAM46C*	*FANCA*	*FANCC*	*FANCD2*	*FANCE*	*FANCF*
FANCG	*FANCL*	*FAS*	*FAT1*	*FBXW7*	*FGF10*	*FGF14*	*FGF19*	*FGF23*	*FGF3*
FGF4	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*	*FGFR4*	*FH*	*FLCN*	*FLT1*	*FLT3*
FLT4	*FOXL2*	*FOXP1*	*FRS2*	*FUBP1*	*GABRA6*	*GATA1*	*GATA2*	*GATA3*	*GATA4*
GATA6	*GID4 (C17orf39)*	*GLI1*	*GNA11*	*GNA13*	*GNAQ*	*GNAS*	*GPR124*	*GRIN2A*	*GRM3*
GSK3B	*H3F3A*	*HGF*	*HNF1A*	*HRAS*	*HSD3B1*	*HSP90AA1*	*IDH1*	*IDH2*	*IGF1R*
IGF2	*IKBKE*	*IKZF1*	*IL7R*	*INHBA*	*INPP4B*	*IRF2*	*IRF4*	*IRS2*	*JAK1*
JAK2	*JAK3*	*JUN*	*KAT6A (MYST3)*	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KEL*
KIT	*KLHL6*	*KMT2A (MLL)*	*KMT2C (MLL3)*	*KMT2D (MLL2)*	*KRAS*	*LMO1*	*LRP1B*	*LYN*	*LZTR1*
MAGI2	*MAP2K1*	*MAP2K2*	*MAP2K4*	*MAP3K1*	*MCL1*	*MDM2*	*MDM4*	*MED12*	*MEF2B*
MEN1	*MET*	*MITF*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH6*	*MTOR*	*MUTYH*
MYC	*MYCL (MYCL1)*	*MYCN*	*MYD88*	*NF1*	*NF2*	*NFE2L2*	*NFKBIA*	*NKX2-1*	*NOTCH1*
NOTCH2	*NOTCH3*	*NPM1*	*NRAS*	*NSD1*	*NTRK1*	*NTRK2*	*NTRK3*	*NUP93*	*PAK3*
PALB2	*PARK2*	*PAX5*	*PBRM1*	*PDCD1LG2*	*PDGFRA*	*PDGFRB*	*PDK1*	*PIK3C2B*	*PIK3CA*
PIK3CB	*PIK3CG*	*PIK3R1*	*PIK3R2*	*PLCG2*	*PMS2*	*POLD1*	*POLE*	*PPP2R1A*	*PRDM1*
PREX2	*PRKAR1A*	*PRKCI*	*PRKDC*	*PRSS8*	*PTCH1*	*PTEN*	*PTPN11*	*QKI*	*RAC1*
RADS0	*RADS1*	*RAF1*	*RANBP2*	*RARA*	*RB1*	*RBM10*	*RET*	*RICTOR*	*RNF43*
ROS1	*RPTOR*	*RUNX1*	*RUNX1T1*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SETD2*	*SF3B1*
SLIT2	*SMAD2*	*SMAD3*	*SMAD4*	*SMARCA4*	*SMARCB1*	*SMO*	*SNCAIP*	*SOCS1*	*SOX10*
SOX2	*SOX9*	*SPEN*	*SPOP*	*SPTA1*	*SRC*	*STAG2*	*STAT3*	*STAT4*	*STK11*
SUFU	*SYK*	*TAF1*	*TBX3*	*TERC*	*TERT (promoter only)*	*TET2*	*TGFBR2*	*TNFAIP3*	*TNFRSF14*
TOP1	*TOP2A*	*TP53*	*TSC1*	*TSC2*	*TSHR*	*U2AF1*	*VEGFA*	*VHL*	*WISP3*
WT1	*XPO1*	*ZBTB2*	*ZNF217*	*ZNF703*					

DNA Gene List: For the Detection of Select Rearrangements

ALK	*BCL2*	*BCR*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*EGFR*	*ETV1*	*ETV4*
ETV5	*ETV6*	*FGFR1*	*FGFR2*	*FGFR3*	*KIT*	*MSH2*	*MYB*	*MYC*	*NOTCH2*
NTRK1	*NTRK2*	*PDGFRA*	*RAF1*	*RARA*	*RET*	*ROS1*	*TMPRSS2*		

An increasing number of SOC treatment options and clinical trials require the knowledge of a molecular alteration



Molecular reports do not present information in an easily clinically actionable format

TUMOR TYPE: STOMACH ADENOCARCINOMA (NOS)

Genomic Alterations Identified†

CDC73 V230fs*28
CIC P1116fs*45
DICER1 C1354fs*1
MLL2 R4904*
MSH2 Q183fs*31
PPP2R1A R183W
RUNX1T1 R458C
SOX9 Q505fs*72

Additional Findings†

Microsatellite status MSI-High
Tumor Mutational Burden TMB-High; 32 Muts/Mb

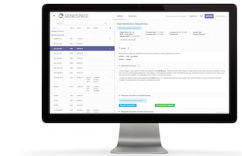
Additional Disease-relevant Genes with No Reportable Alterations Identified†

ERBB2

Sarah Cannon's Personalized Medicine program is uniquely positioned to address the opportunities for our partnered medical oncologists, molecular profiling vendors, and pharmaceutical industry partners

GENOSPACE: ENABLING THE CONVERGENCE OF CLINICAL RESEARCH AND CLINICAL CARE

Large-scale clinical-genomic data aggregation

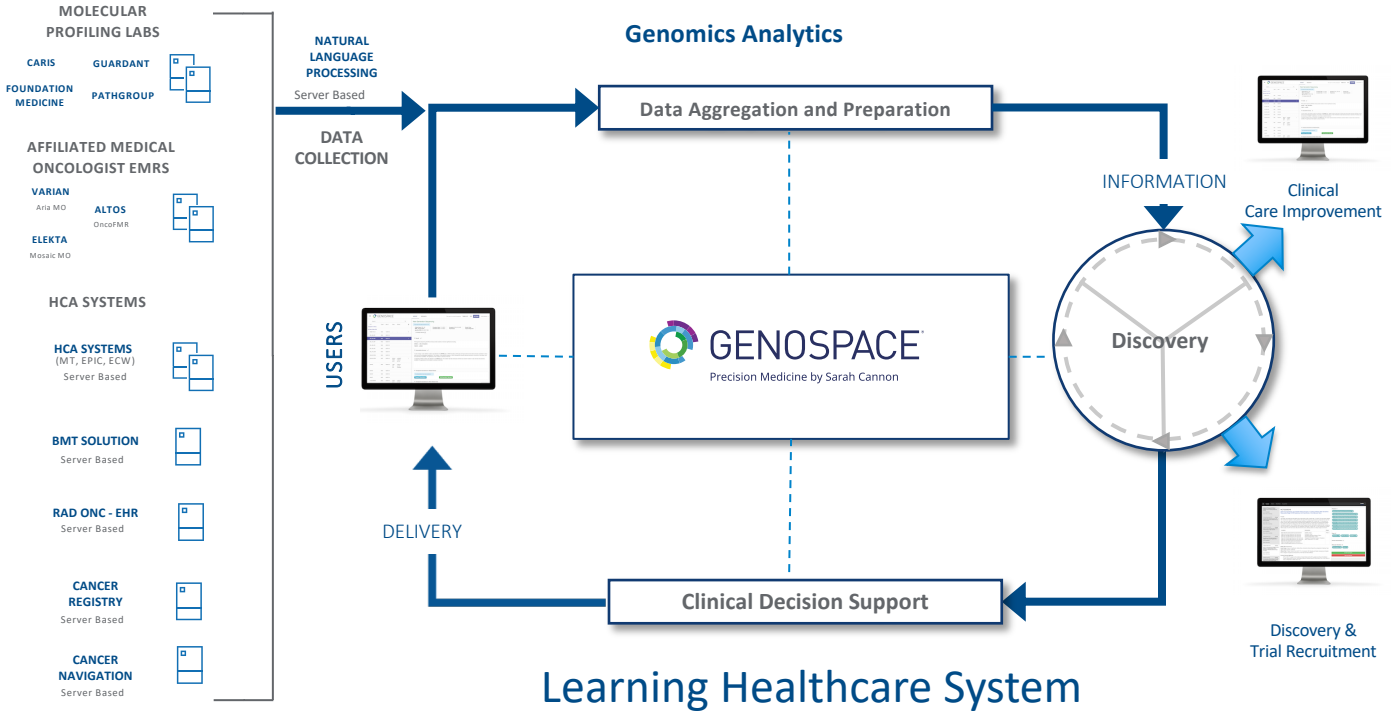


Clinical Decision Support

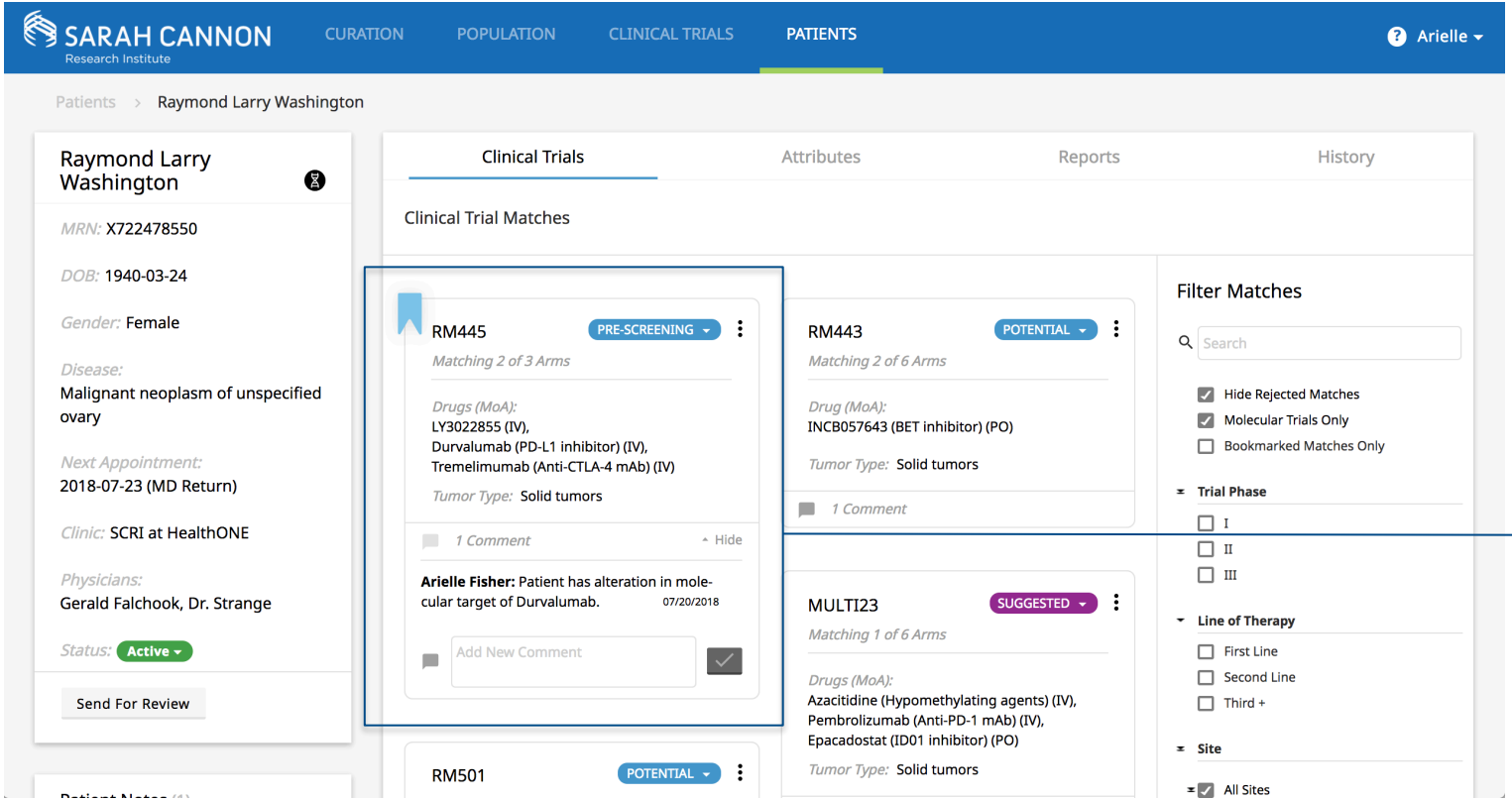
Discovery & Trial Recruitment

SARAH CANNON
Research Institute

GENOSPACE: ENABLING THE CONVERGENCE OF CLINICAL RESEARCH AND CLINICAL CARE



REVIEW AND MANAGE YOUR PATIENT'S THERAPY OPTIONS

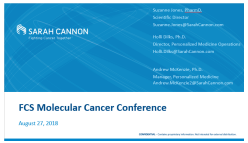


Annotate patient-trial matches to communicate with other clinical users

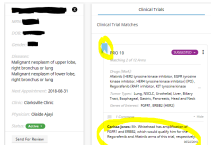
MOLECULAR ONCOLOGY SUPPORT SERVICES

Molecular Cancer Conferences

- **Regularly-occurring office-specific teleconference**
- >1000 MCC reviews in 12 months
- ~18% enrollment rate
- >2x increase in MP ordering
- ~23 physician-hours/month



Molecular Oncology Support Services



Personalized Molecular Insights

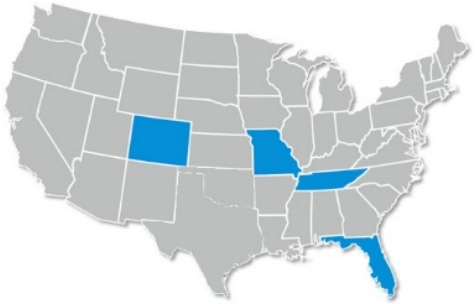
Powered by Genospace

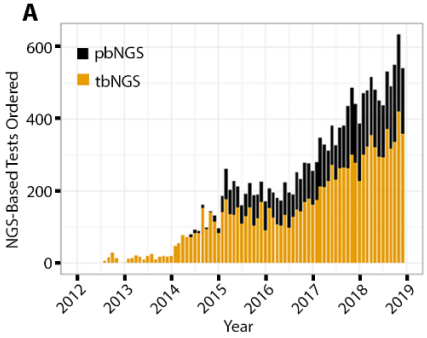
- **Real-time Patient-level review of molecular profiles:**
- Since 8/6/2018, All new molecular profiles from late-phase clinics at TO have been annotated in Genospace and abstracted into Personalized Medicine Data Warehouse

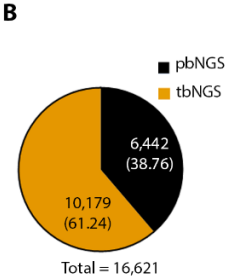
"On-Call" Molecular Insights

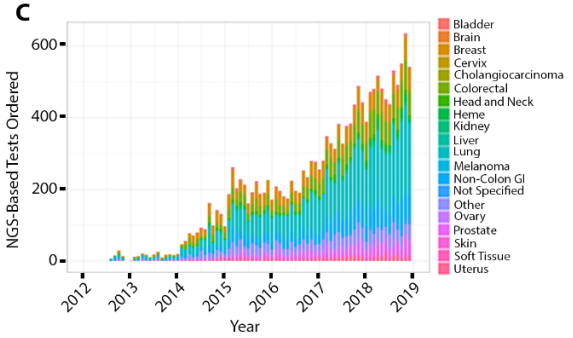
- ***Ad hoc* (concierge-level) germline and somatic mutational analysis**
- ~4-5 *ad hoc* cases/week from FCS and TO

BACKGROUND: SARAH CANNON & MOLECULAR PROFILING









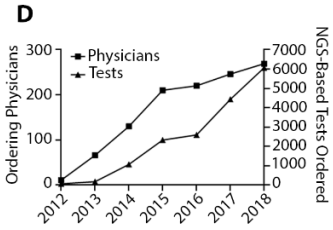
Data Availability:

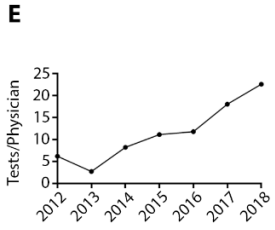
Strategic Sites

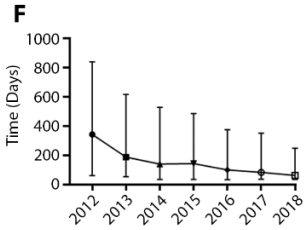
- Tennessee Oncology, Nashville
- Tennessee Oncology, Chattanooga
- Florida Cancer Specialists-East, West Palm Beach
- Florida Cancer Specialists-North, St. Petersburg
- Florida Cancer Specialists-Panhandle, Tallahassee
- Florida Cancer Specialists-South, Ft. Myers
- HCA Midwest Health, Kansas City

DDU/Phase 1

- Sarah Cannon, Denver
- Florida Cancer Specialists, Sarasota
- Tennessee Oncology, Nashville





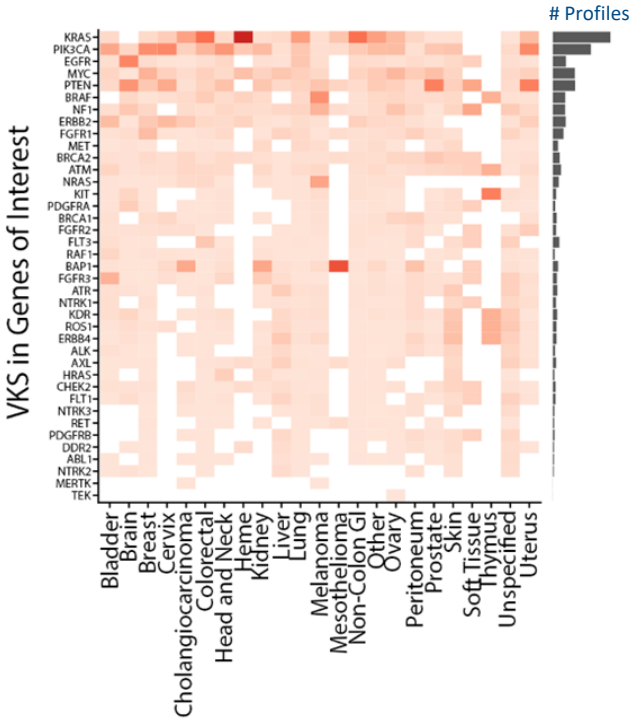


Rapid adoption of tissue- and plasma-based NGS from private medical oncology practices

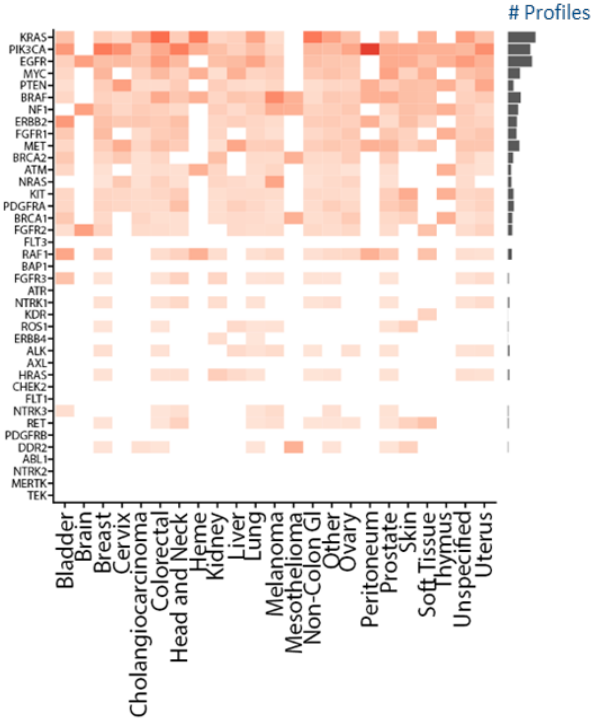
SARAH CANNON
Fighting Cancer Together™

MUTATION ANALYSIS OF TISSUE-BASED NGS AND PLASMA-BASED NGS

TISSUE-BASED NGS



PLASMA-BASED NGS

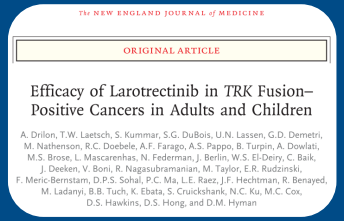


SARAH CANNON
Research Institute

TWO TRENDS, ONE TRIAGE DECISION

Precision Medicine

Immuno-Oncology

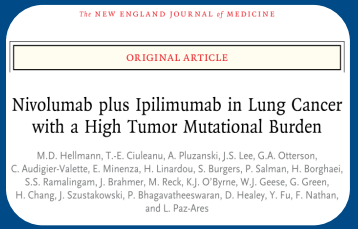

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* Fusion–Positive Cancers in Adults and Children

A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman

NGS Profiling


The NEW ENGLAND JOURNAL of MEDICINE

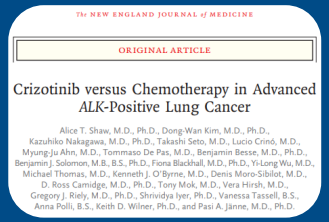
ORIGINAL ARTICLE

Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden

M.D. Hellmann, T.-E. Ciuleanu, A. Pluzanski, J.S. Lee, G.A. Otterson, C. Audigier-Valette, E. Minenza, H. Linardou, S. Burgers, P. Salman, H. Borghaei, S.S. Ramalingam, J. Brahmer, M. Reck, K.J. O'Byrne, W.J. Geese, G. Green, H. Chang, J. Szustakowski, P. Bhagavatheeswaran, D. Healey, Y. Fu, F. Nathan, and L. Paz-Ares

Actionable Genomic Alterations

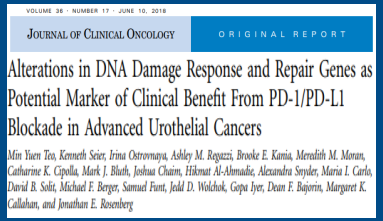
MSI, TMB, DDR


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Crizotinib versus Chemotherapy in Advanced *ALK*-Positive Lung Cancer

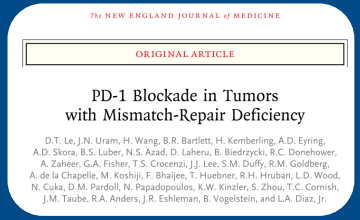
Alice T. Shaw, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Ph.D., Takashi Seto, M.D., Lucio Crinò, M.D., Myung-Ju Ahn, M.D., Tommaso De Pas, M.D., Benjamin Besse, M.D., Ph.D., Benjamin J. Solomon, M.B., B.S., Ph.D., Fiona Blackhall, M.D., Ph.D., Yi-Long Wu, M.D., Michael Thomas, M.D., Kenneth J. O'Byrne, M.D., Denis Moro-Sibilot, M.D., D. Ross Camidge, M.D., Ph.D., Tony Mok, M.D., Vera Hirsh, M.D., Gregory J. Riely, M.D., Ph.D., Shrividya Iyer, Ph.D., Vanessa Tassell, B.S., Anna Polli, B.S., Keith D. Wilner, Ph.D., and Pasi A. Jänne, M.D., Ph.D.


VOLUME 36 · NUMBER 17 · JUNE 10, 2018

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Alterations in DNA Damage Response and Repair Genes as Potential Marker of Clinical Benefit From PD-1/PD-L1 Blockade in Advanced Urothelial Cancers

Min Yuen Teo, Kenneth Seier, Irina Ostrovnaya, Ashley M. Regazzi, Brooke E. Kania, Meredith M. Moran, Catharine K. Cipolla, Mark J. Bluth, Joshua Chaim, Hikmat Al-Ahmadie, Alexandra Snyder, Maria I. Carlo, David B. Solit, Michael F. Berger, Samuel Funt, Jedd D. Wolchok, Gopa Iyer, Dean F. Bajorin, Margaret K. Callahan, and Jonathan E. Rosenberg


The NEW ENGLAND JOURNAL of MEDICINE

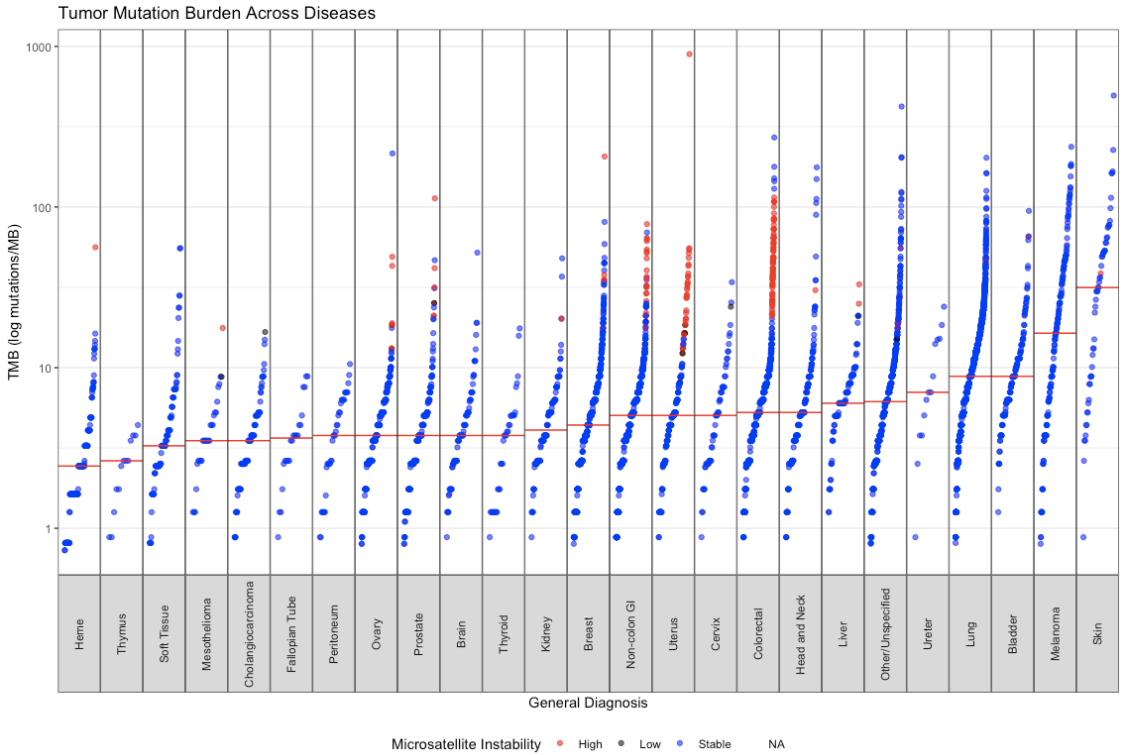
ORIGINAL ARTICLE

PD-1 Blockade in Tumors with Mismatch-Repair Deficiency

D.T. Le, J.N. Uram, H. Wang, B.R. Bartlett, H. Kemberling, A.D. Eyring, A.D. Skora, B.S. Luber, N.S. Azad, D. Laheru, B. Biedrzycki, R.C. Donehower, A. Zaheer, G.A. Fisher, T.S. Crocenzi, J.J. Lee, S.M. Duffy, R.M. Goldberg, A. de la Chapelle, M. Koshiji, F. Bhaijee, T. Huebner, R.H. Hruban, L.D. Wood, N. Cuka, D.M. Pardoll, N. Papadopoulos, K.W. Kinzler, S. Zhou, T.C. Cornish, J.M. Taube, R.A. Anders, J.R. Eshleman, B. Vogelstein, and L.A. Diaz, Jr.

SARAH CANNON
Research Institute

TMB FROM COMMERCIAL NGS VENDORS IN THE COMMUNITY SETTING

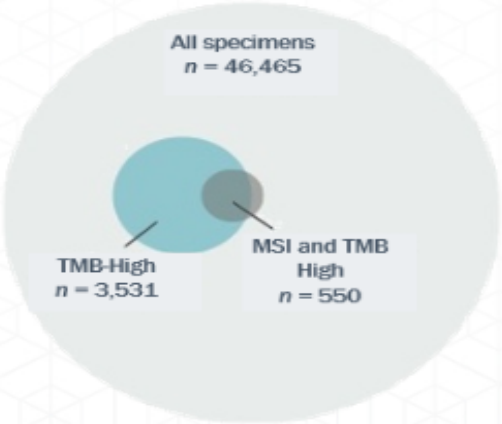


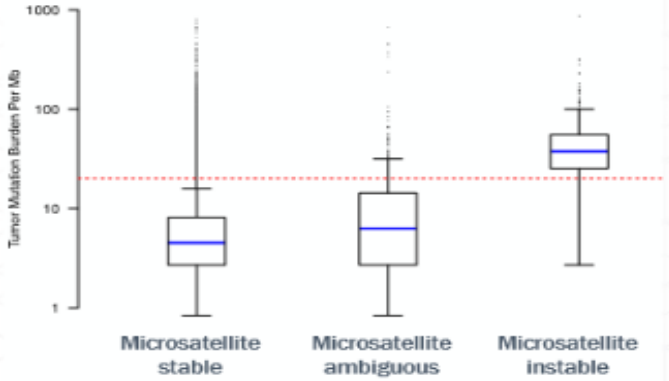
TMB across tumor types in Sarah Cannon data largely mirrors data from previous reports.

SARAH CANNON
Fighting Cancer Together™

MSI-HIGH SPECIMENS ARE A SUBSET OF HIGH TMB SPECIMENS (N = 46,465)

- The majority of MSI-H specimens (~84%) are TMB-H, but not the reverse
  - Only 14.5% of TMB-H specimens are also MSI-H





FOUNDATION MEDICINE

ZR Chalmers et al, In Press

P Stephens AACR 2017

SARAH CANNON
Research Institute

FIRST TISSUE AGNOSTIC FDA APPROVAL---MISMATCH REPAIR DEFICIENCY

FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication

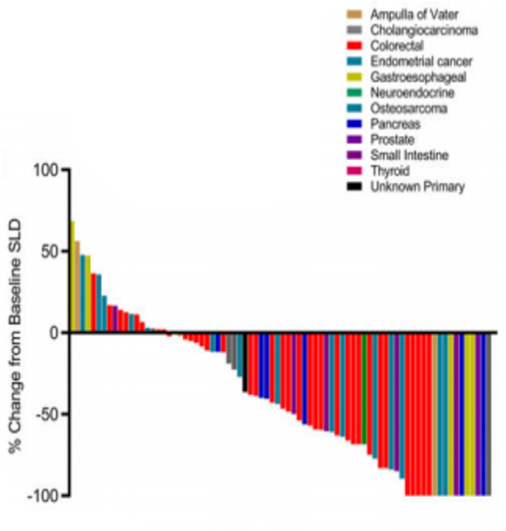
Listen to the FDA D.I.S.C.O. podcast about this approval

On May 23, 2017, the U.S. Food and Drug Administration granted accelerated approval to pembrolizumab (KEYTRUDA, Merck & Co.) for adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options or with MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

This is the FDA's first tissue/site-agnostic approval.

The approval was based on data from 149 patients with MSI-H or dMMR cancers enrolled across five uncontrolled, multi-cohort, multi-center, single-arm clinical trials. Ninety patients had colorectal cancer and 59 patients were diagnosed with one of 14 other cancer types. Patients received either pembrolizumab, 200 mg every 3 weeks, or pembrolizumab, 10 mg/kg every 2 weeks. Treatment continued until unacceptable toxicity, or disease progression that was either symptomatic, rapidly progressive, required urgent intervention, or associated with a decline in performance status. A maximum of 24 months of treatment was administered.

The major efficacy outcome measures were objective response rate (ORR) assessed by blinded independent central radiologists' review according to RECIST 1.1, and response duration. ORR was 39.6% (95% CI: 31.7, 47.9). Responses lasted six months or more for 78% percent of those who responded to pembrolizumab. There were 11 complete responses and 48 partial responses. ORR was similar irrespective of whether patients were diagnosed with CRC (36%) or a different cancer type (46% across the 14 other cancer types).



Objective response: 53%

Complete response: 21%

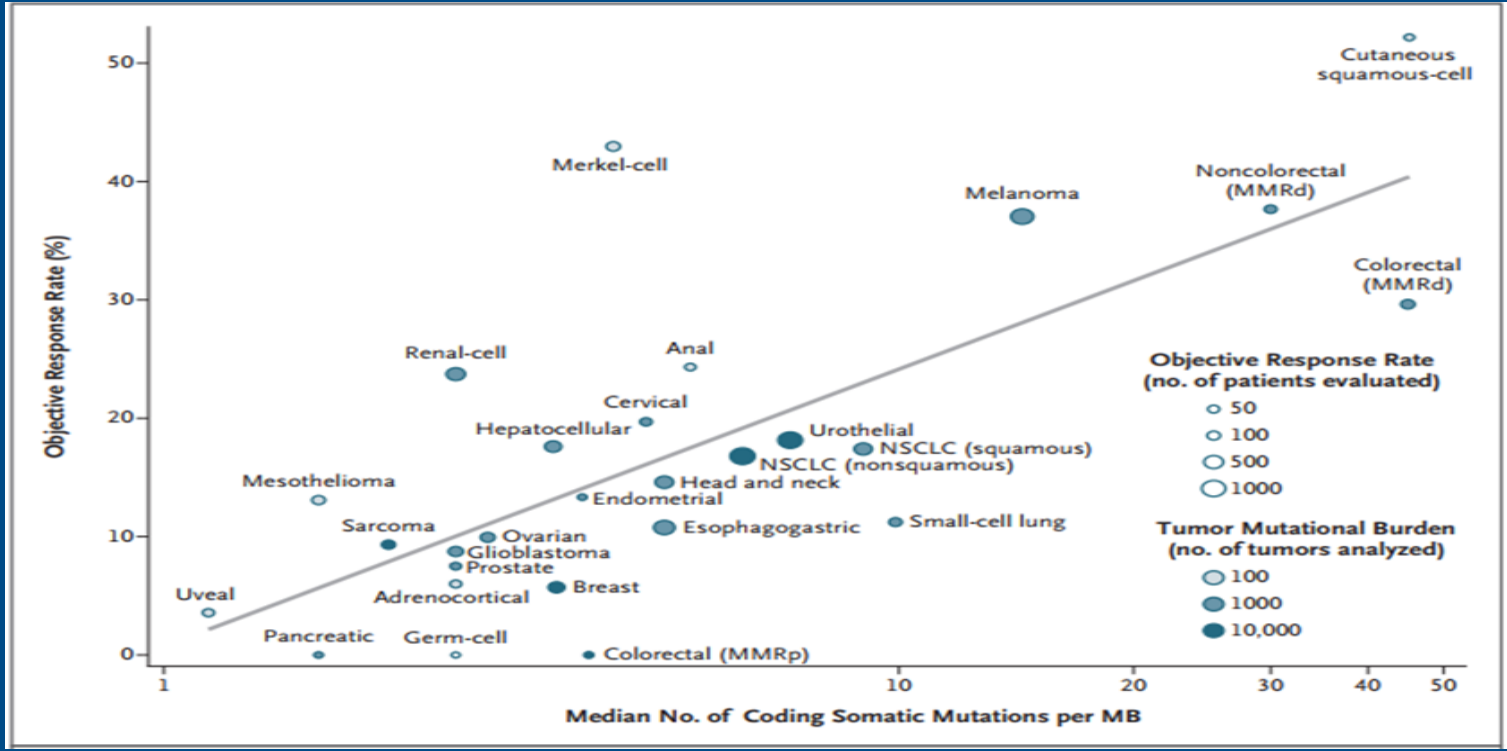
Disease control rate: 77%

Median PFS and OS not yet reached (median follow up 12.5 months)

Le et al. Science 2017 July 28;357 (6349): 409 - 413

SARAH CANNON Research Institute

CORRELATION BETWEEN TMB AND RESPONSE RATE TO PD1-INHIBITION



SARAH CANNON
Research Institute

Yarchoan et al. NEJM 2017;377;25:2500-2501

TMB STILL AN INVESTIGATIONAL BIOMARKER FOR NSCLC?

KEYNOTE 189 and KEYNOTE 21 both demonstrated TMB not significantly associated with OS, PFS, or ORR

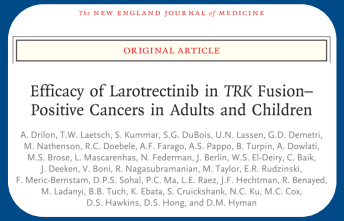
Garassino et al. Abstract OA04.06
Langer et al. Abstract OA04.05

SARAH CANNON Research Institute

TWO TRENDS, ONE TRIAGE DECISION

Precision Medicine

Immuno-Oncology

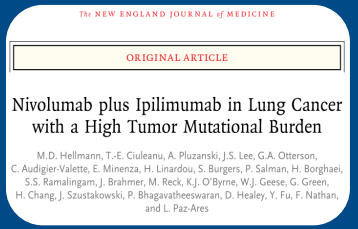

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* Fusion–Positive Cancers in Adults and Children

A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman

NGS Profiling


The NEW ENGLAND JOURNAL of MEDICINE

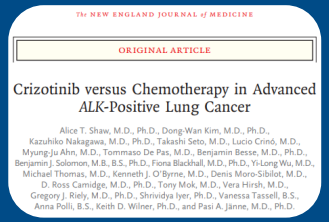
ORIGINAL ARTICLE

Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden

M.D. Hellmann, T.-E. Ciuleanu, A. Pluzanski, J.S. Lee, G.A. Otterson, C. Audigier-Valette, E. Minenza, H. Linardou, S. Burgers, P. Salman, H. Borghaei, S.S. Ramalingam, J. Brahmer, M. Reck, K.J. O'Byrne, W.J. Geese, G. Green, H. Chang, J. Szustakowski, P. Bhagavatheeswaran, D. Healey, Y. Fu, F. Nathan, and L. Paz-Ares

Actionable Genomic Alterations

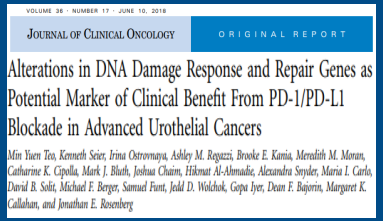
MSI, TMB, DDR


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Crizotinib versus Chemotherapy in Advanced *ALK*-Positive Lung Cancer

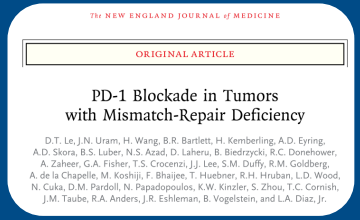
Alice T. Shaw, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Ph.D., Takashi Seto, M.D., Lucio Crinò, M.D., Myung-Ju Ahn, M.D., Tommaso De Pas, M.D., Benjamin Besse, M.D., Ph.D., Benjamin J. Solomon, M.B., B.S., Ph.D., Fiona Blackhall, M.D., Ph.D., Yi-Long Wu, M.D., Michael Thomas, M.D., Kenneth J. O'Byrne, M.D., Denis Moro-Sibilot, M.D., D. Ross Camidge, M.D., Ph.D., Tony Mok, M.D., Vera Hirsh, M.D., Gregory J. Riely, M.D., Ph.D., Shrividya Iyer, Ph.D., Vanessa Tassell, B.S., Anna Polli, B.S., Keith D. Wilner, Ph.D., and Pasi A. Jänne, M.D., Ph.D.


VOLUME 36 · NUMBER 17 · JUNE 10, 2018

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Alterations in DNA Damage Response and Repair Genes as Potential Marker of Clinical Benefit From PD-1/PD-L1 Blockade in Advanced Urothelial Cancers

Min Yuen Teo, Kenneth Seier, Irina Ostrovnaya, Ashley M. Regazzi, Brooke E. Kania, Meredith M. Moran, Catharine K. Cipolla, Mark J. Bluth, Joshua Chaim, Hikmat Al-Ahmadie, Alexandra Snyder, Maria I. Carlo, David B. Solit, Michael F. Berger, Samuel Funt, Jedd D. Wolchok, Gopa Iyer, Dean F. Bajorin, Margaret K. Callahan, and Jonathan E. Rosenberg


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

PD-1 Blockade in Tumors with Mismatch-Repair Deficiency

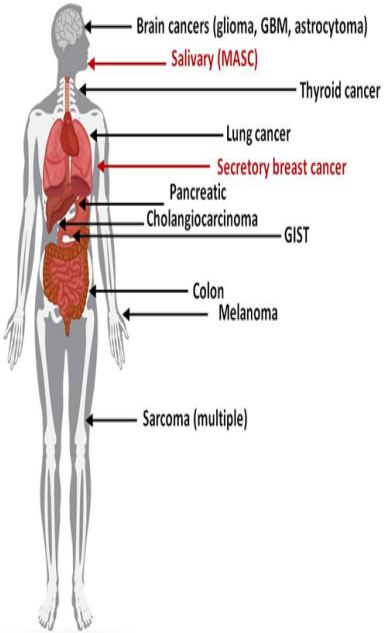
D.T. Le, J.N. Uram, H. Wang, B.R. Bartlett, H. Kemberling, A.D. Eyring, A.D. Skora, B.S. Luber, N.S. Azad, D. Laheru, B. Biedrzycki, R.C. Donehower, A. Zaheer, G.A. Fisher, T.S. Crocenzi, J.J. Lee, S.M. Duffy, R.M. Goldberg, A. de la Chapelle, M. Koshiji, F. Bhaijee, T. Huebner, R.H. Hruban, L.D. Wood, N. Cuka, D.M. Pardoll, N. Papadopoulos, K.W. Kinzler, S. Zhou, T.C. Cornish, J.M. Taube, R.A. Anders, J.R. Eshleman, B. Vogelstein, and L.A. Diaz, Jr.

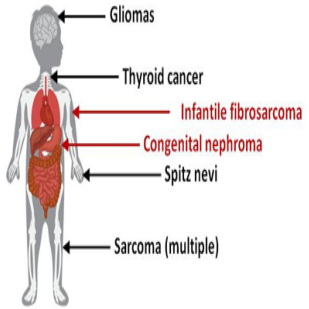
SARAH CANNON
Research Institute

WHAT TARGETED THERAPIES HAVE BEEN APPROVED FOR SPECIFIC TYPES OF CANCER? (WWW.CANCER.GOV)

- Brain cancer: Bevacizumab (Avastin®), everolimus (Afinitor®)
- Breast cancer: Everolimus (Afinitor®), lapatinib (Tykerb®), trastuzumab (Herceptin®), fulvestrant (Faslodex®), goserelin acetate (Zoladex®), leuprolide acetate (Eligard®), anastrozole (Arimidex®), exemestane (Aromasin®), lapatinib (Tykerb®), letrozole (Femara®), pertuzumab (Perjeta®), ado-trastuzumab emtansine (Kadcyla®), palbociclib (Ibrance®), ribociclib (Kisqali®), neratinib maleate (Nerlynx™), abemaciclib (Verzenio™), olaparib (Lynparza™)
- Cervical cancer: Bevacizumab (Avastin®)
- Colorectal cancer: Cetuximab (Erbitux®), panitumumab (Vectibix®), bevacizumab (Avastin®), ziv-aflibercept (Zaltrap®), regorafenib (Stivarga®), ramucirumab (Cyramza®), nivolumab (Opdivo®)
- Dermatofibrosarcoma protuberans: Imatinib mesylate (Gleevec®)
- Endocrine/neuroendocrine tumors: Lanreotide acetate (Somatuline® Depot), avelumab (Bavencio®), lutetium Lu 177-dotatate (Lutathera®)
- Head and neck cancer: Cetuximab (Erbitux®), pembrolizumab (Keytruda®), nivolumab (Opdivo®)
- Gastrointestinal stromal tumor: Imatinib mesylate (Gleevec®), sunitinib (Sutent®), regorafenib (Stivarga®)
- Giant cell tumor of the bone: Denosumab (Xgeva®)
- Kidney cancer: Bevacizumab (Avastin®), sorafenib (Nexavar®), sunitinib (Sutent®), pazopanib (Votrient®), temsirolimus (Torisel®), everolimus (Afinitor®), axitinib (Inlyta®), nivolumab (Opdivo®), cabozantinib (Cabometyx™), lenvatinib mesylate (Lenvima®), ipilimumab (Yervoy®)
- Leukemia: Tretinoin (Vesanoid®), imatinib mesylate (Gleevec®), dasatinib (Sprycel®), nilotinib (Tasigna®), bosutinib (Bosulif®), rituximab (Rituxan®), alemtuzumab (Campath®), ofatumumab (Arzerra®), obinutuzumab (Gazyva®), ibrutinib (Imbruvica®), idelalisib (Zydelig®), blinatumomab (Blincyto®), venetoclax (Venclexta™), ponatinib hydrochloride (Iclusig®), midostaurin (Rydapt®), enasidenib mesylate (Idhifa®), inotuzumab ozogamicin (Besponsa®), tisagenlecleucel (Kymriah®), gemtuzumab ozogamicin (Mylotarg™), rituximab and hyaluronidase human (Rituxan Hycela™)
- Liver cancer: Sorafenib (Nexavar®), regorafenib (Stivarga®), nivolumab (Opdivo®)
- Lung cancer: Bevacizumab (Avastin®), crizotinib (Xalkori®), erlotinib (Tarceva®), gefitinib (Iressa®), afatinib dimaleate (Gilotrif®), ceritinib (LDK378/Zykadia™), ramucirumab (Cyramza®), nivolumab (Opdivo®), pembrolizumab (Keytruda®), osimertinib (Tagrisso™), necitumumab (Portrazza™), ceritinib (Alecensa®), atezolizumab (Tecentriq™), brigatinib (Alunbrig™), trametinib (Mekinist®), dabrafenib (Tafinlar®), durvalumab (Imfinzi™)
- Lymphoma: Ibritumomab tiuxetan (Zevalin®), denileukin diftitox (Ontak®), brentuximab vedotin (Adcetris®), rituximab (Rituxan®), vorinostat (Zolinza®), romidepsin (Istodax®), bexarotene (Targretin®), bortezomib (Velcade®), pralatrexate (Folotyn®), ibrutinib (Imbruvica®), siltuximab (Sylvant®), idelalisib

TUMOR AGNOSTIC FDA APPROVAL--- LAROTRECTINIB (NTRK FUSION)

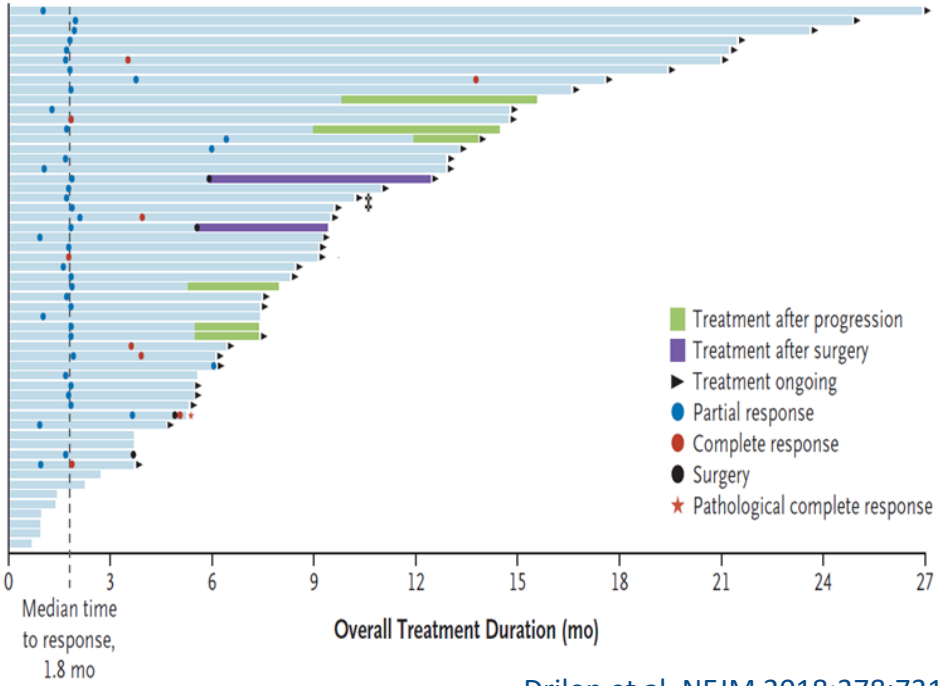




Common cancer with low TRK fusion frequency

Rare cancer with high TRK fusion frequency

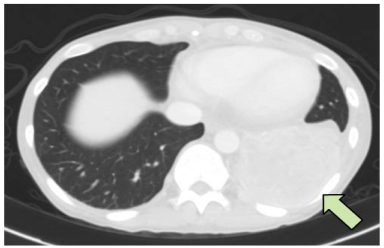
Estimated 1,500–5,000 patients harbor TRK fusion-positive cancers in the United States annually

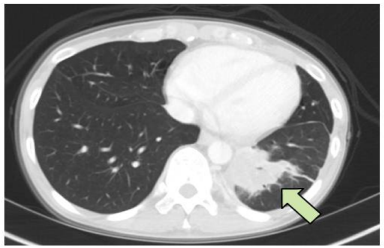


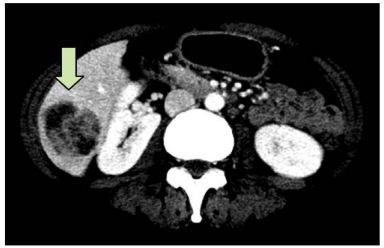
Drilon et al. NEJM 2018;378:731-9.

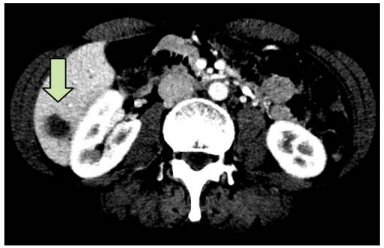
FDA APPROVED
November 26, 2018

SARAH CANNON
Research Institute









Baseline

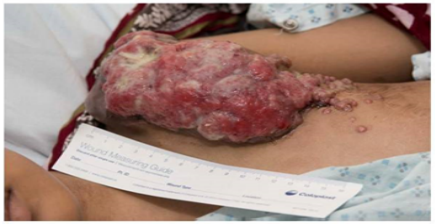
Cycle 4

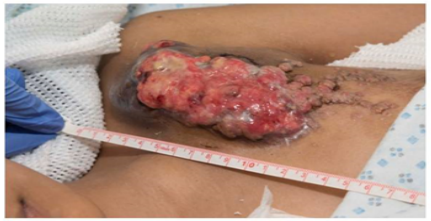
45F NSCLC & paraneoplastic hypertrophic osteoarthropathy

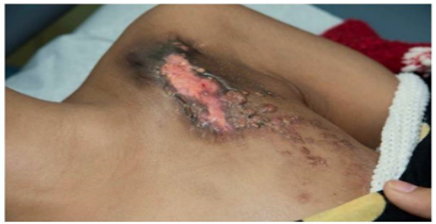
Prior therapy: platinum/pemetrexed

Larotrectinib ongoing in month 8, resolution of paraneoplastic symptoms

FDA APPROVED
November 26, 2018







Baseline

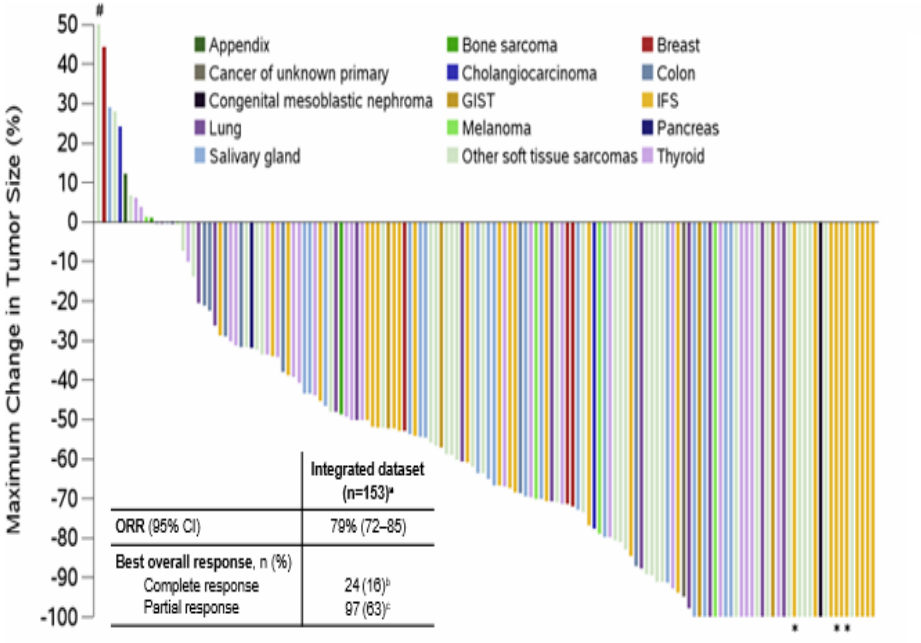
Day 6

Day 20

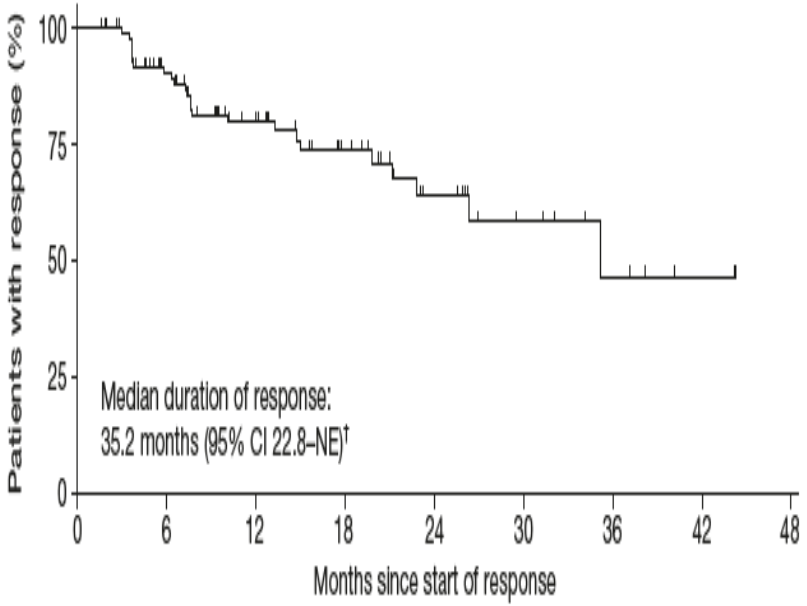
14F, prior therapy: 4 lines of chemotherapy and repeated resections
Treated with larotrectinib under expanded access

Presented By David Hyman at 2017 ASCO Annual Meeting

EXPANDED LAROTRECTINIB RESPONSE AND DURABILITY OF RESPONSE



	Integrated dataset (n=153)[a]
ORR (95% CI)	79% (72–85)
Best overall response, n (%)	
Complete response	24 (16)[b]
Partial response	97 (63)[c]



SARAH CANNON
Research Institute

Hyman et al. ESMO 2019 Abstract 445PD.

TISSUE AGNOSTIC FDA APPROVAL--- ENTRECTINIB (NTRK FUSION)

Regulatory Focus™

Regulatory Focus™ > News Articles > 2019 > 8 > FDA Offers Accelerated Approval for 3rd Tissue-Agnostic Cancer Treatment

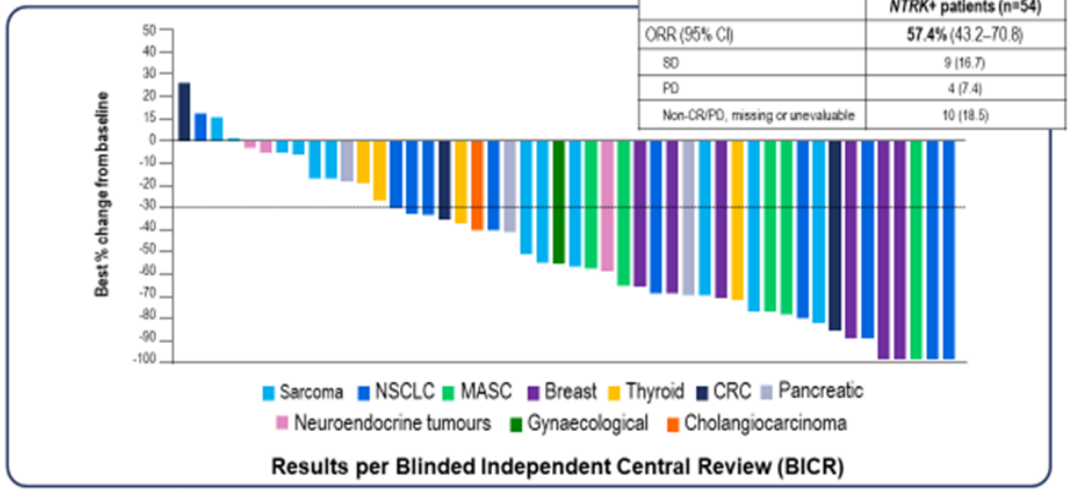
FDA Offers Accelerated Approval for 3rd Tissue-Agnostic Cancer Treatment

Posted 15 August 2019 | By Zachary Brennan

FDA APPROVED
August 15, 2019

Entrectinib activity in *NTRK* fusion-positive solid tumours: individual patient responses by tumour type

	NTRK+ patients (n=54)
ORR (95% CI)	**57.4%** (43.2–70.8)
SD	9 (16.7)
PD	4 (7.4)
Non-CR/PD, missing or unevaluable	10 (18.5)



MUNICH 2018 ESMO congress

Cut-off date: 31 May 2018
Note: Patients (n=6) without matched pre/post therapy scans were excluded from the plot
CI: confidence interval; CRC: colorectal cancer; MASC: mammary analogue secretory carcinoma; NSCLC: non-small cell lung cancer

Demetri GD et al. ESMO 2018

SARAH CANNON Research Institute

HEALTH NEWS SEPTEMBER 6, 2019 / 12:58 AM / 8 DAYS AGO

REUTERS

Inside drugmakers' strategy to boost cancer medicines with 'Lazarus effect'

According to Dr. Brian Alexander, chief medical officer of Roche's gene testing company Foundation Medicine, only about 15% of U.S. patients with advanced cancers get comprehensive genomic profiling. Another 25% get single-gene testing, he said, and a large proportion "are not getting any testing at all."

At MD Anderson, which sees 100,000 new cancer patients a year, only around 10,000 eventually have their tumors sequenced.

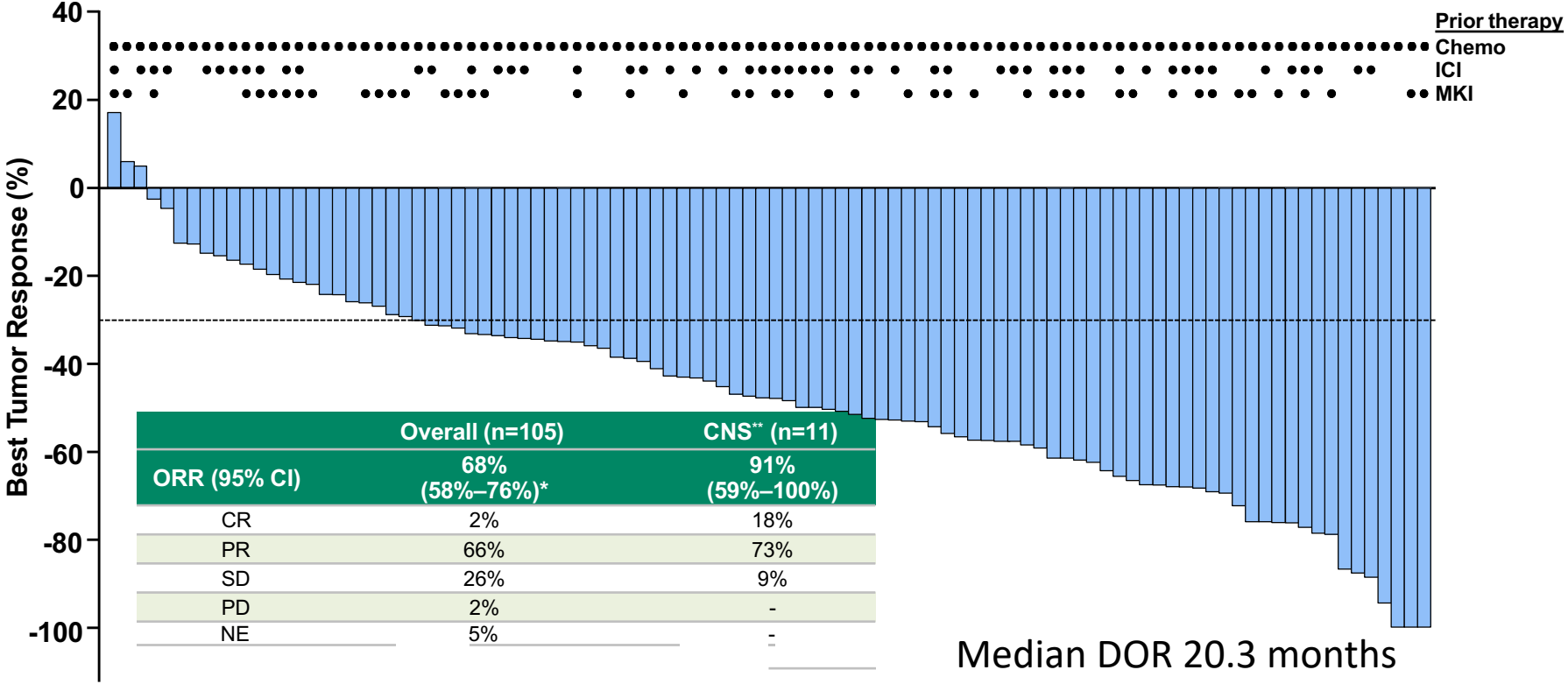
IASLC
2019 World Conference on Lung Cancer
September 7–10, 2019 | Barcelona, Spain
wclc2019.iaslc.com | #WCLC19
Conquering Thoracic Cancers Worldwide

Registrational Results of LIBRETTO-001: A Phase 1/2 Trial of Selpercatinib (LOXO-292) in Patients with *RET* Fusion-Positive Lung Cancers

A. Drilon[1], G. Oxnard[2], L. Wirth[3], B. Besse[4], O. Gautschi[5], S.W.D. Tan[6], H. Loong[7], T. Bauer[8], Y.J. Kim[9], A. Horiike[10], K. Park[11], M. Shah[12], C. McCoach[13], L. Bazhenova[14], T. Seto[15], M. Brose[16], N. Pennell[17], J. Weiss[18], I. Matos[19], N. Peled[20], B.C. Cho[21], Y. Ohe[22], K. Reckamp[23], V. Boni[24], M. Satouchi[25], G. Falchook[26], W. Akerley[27], H. Daga[28], T. Sakamoto[29], J. Patel[30], N. Lakhani[31], F. Barlesi[32], M. Burkard[33], V. Zhu[34], V. Moreno Garcia[35], J. Medioni[36], M. Matrana[37], C. Rolfo[38], D.H. Lee[39], H. Nechushtan[40], M. Johnson[41], V. Velcheti[42], M. Nishio[43], R. Toyozawa[44], K. Ohashi[45], L. Song[46], J. Han[47], A. Spira[48], M.Duca[49], K. Staal Rohrberg[50], S. Takeuchi[51], J. Sakakibara[52], S. Waqar[53], H. Kenmotsu[54], F. Wilson[55], B.Nair[56], E. Olek[56], J. Kherani[56], K. Ebata[56], E. Zhu[56], M. Nguyen[56], L. Yang[56], X. Huang[56], S. Cruickshank[56], S. Rothenberg[56], B. Solomon[57], K. Goto[58], V. Subbiah[59]

1.Memorial Sloan Kettering Cancer Center, New York, NY/United States of America. 2. Dana-Farber Cancer Institute, Boston, MA/United States of America. 3. Massachusetts General Hospital, Boston, MA/United States of America. 4. Institut Gustav Roussy, Villejuif/France. 5. Luzerner General Hospital, Luzern/Switzerland. 6. National Cancer Centre, Singapore/Singapore. 7. Prince of Wales Hospital, Shatin/Hong Kong PRC. 8. Sarah Cannon Research Institute, Nashville, TN/United States of America. 9. Seoul National University Bundang Hospital, Gyeonggido/ Democratic People's Republic of Korea. 10. The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo/Japan. 11. Samsung Medical Center, Seoul/Democratic People's Republic of Korea. 12. The Ohio State University, Columbus, OH/United States of America. 13. University of California, San Francisco, CA/United States of America. 14. University of California San Diego, Moores Cancer Center, La Jolla, CA/United States of America. 15. National Hospital Organization Kyushu Cancer Center, Fukuoka/Japan. 16. University of Pennsylvania, Philadelphia, PA/United States of America. 17. Cleveland Clinic, Cleveland, OH/United States of America. 18. University of North Carolina, Chapel Hill, NC/United States of America. 19. Vall d' Hebron Institute of Oncology, Barcelona/Spain. 20. Soroka Medical Center, Beer Sheva/Israel. 21. Severance Hospital, Yonsei University Health System, Seoul/ Democratic People's Republic of Korea. 22. National Cancer Center Hospital, Tokyo/Japan. 23. City of Hope Comprehensive Cancer Center, Duarte, CA/United States of America. 24. START Madrid-CIOCC, Madrid/Spain. 25. Hyogo Cancer Center, Akashi/Japan. 26.Sarah Cannon Research Institute, Denver, CO/United States of America. 27. Huntsman Cancer Institute, Salt Lake City, UT/United States of America. 28. Osaka City General Hospital, Osaka/Japan. 29. Tottori University Hospital, Yonago/Japan. 30. University of Chicago, Chicago, IL/United States of America. 31. South Texas Accelerated Research Therapeutics (START) Midwest, Grand Rapids, MI/United States of America. 33. University of Wisconsin - Carbone Cancer Center, Madison, WI/United States of America. 34 University of California - Irvine Medical Center, Irvine, CA/United States of America. 35. Fundacion Jimenez Diaz, START-Madrid-FJD, Madrid/Spain. 36. Hopital Europeen Georges Pompidou, Paris/France. 37. Ochsner Clinic Foundation, New Orleans, LA/United States of America. 38. University of Maryland Medical Center, Baltimore, MD/United States of America. 39. Asan Medical Center, Seoul/ Democratic People's Republic of Korea. 40. Hadassah Hebrew University Medical Center Ein Karem, Jerusalem/Israel. 41. Tennesse Oncology/Sarah Cannon Research Institute, Nashville, TN/United States of America. 42. NYU Langone Cancer Center, New York, NY/United States of America. 43. Cancer Institute Hospital of JFCR, Tokyo/Japan. 44. National Hospital Organization Kyushu Cancer Center, Fukuoka/Japan. 45. Okayama University Hospital, Okayama/Japan. 46. Kaiser Permanente - Santa Clara, CA/ United States of America. 47. National Cancer Center, Democratic People's Republic of Korea. 48. Virginia Cancer Specialists, VA/United States of America. 49. Istituto Nazionale Tumori - National Cancer Institute, Milan, Italy. 50. The Finsen Centre, Rigshospitalet, Denmark. 51. Kanazawa University Hospital, Kanazawa, Japan. 52. Hokkaido University Hospital, Hokkaido, Japan. 53. Washington University School of Medicine, Missouri/United States of America. 54. Shizuoka Cancer Center, Nagaizumi, Japan. 55. Yale University School of Medicine - Yale Cancer Center, CT/United States of America. 56. Loxo Oncology, Inc., a wholly owned subsidiary of Eli Lilly and Company, Stamford, CT/United States of America. 57. Peter MacCallum Cancer Center, Melbourne, ACT/Australia. 58. National Cancer Center Hospital East, Kashiwa/Japan. 59. MD Anderson Cancer Center, Houston, TX/United States of America

Efficacy of Selpercatinib: Primary Analysis Set (n=105)



	Overall (n=105)	CNS** (n=11)
ORR (95% CI)	68% (58%–76%)*	91% (59%–100%)
CR	2%	18%
PR	66%	73%
SD	26%	9%
PD	2%	-
NE	5%	-

Median DOR 20.3 months

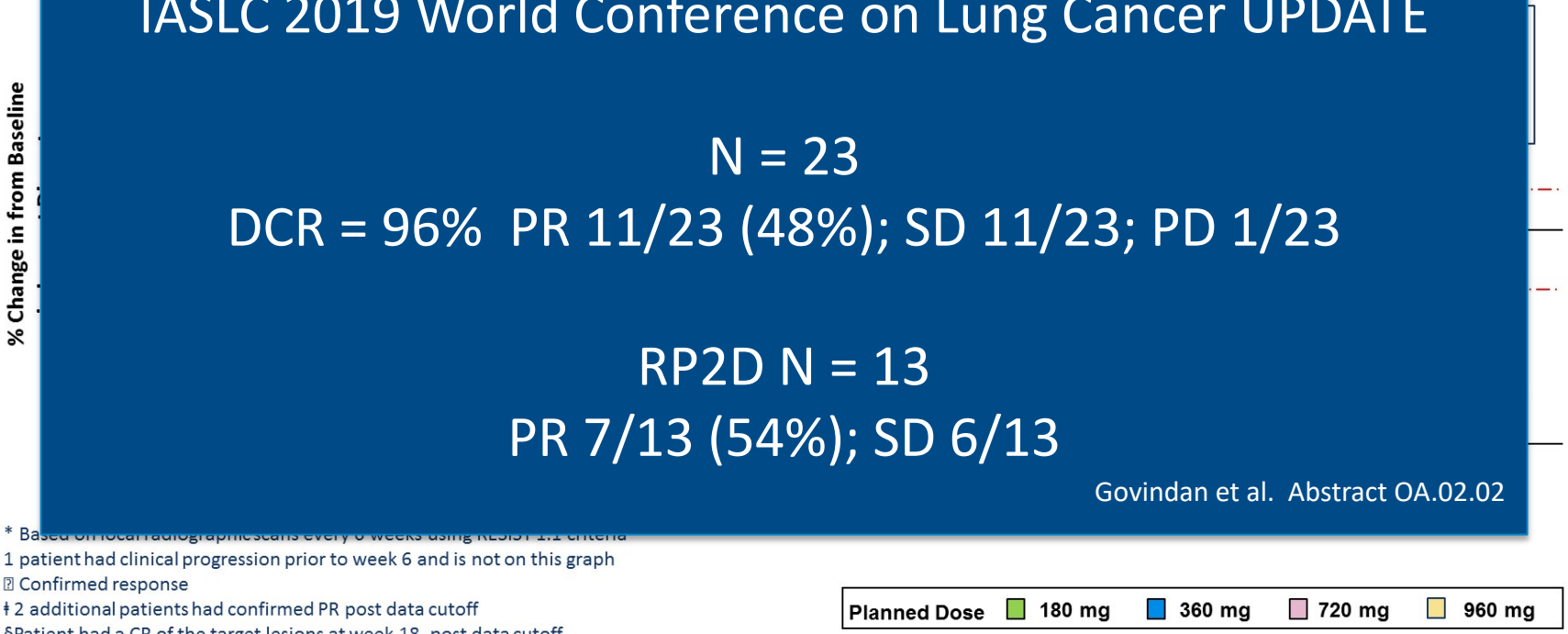
Investigator response assessments as of June 17th, 2019. 5 patients not shown in waterfall plot: 3 discontinued prior to any post-baseline imaging assessments, 1 did not have measurable disease at baseline, and 1 deemed not evaluable on study by the Investigator. NE—Not evaluable, n=5 patients: 3 discontinued prior to any post-baseline imaging assessments, 1 deemed not evaluable on study by the Investigator, and 1 discontinued after a single post-baseline imaging assessment showing SD, less than 6 weeks after starting treatment. Total % may be different than the sum of the individual due to rounding. *N=105 dataset includes 2 unconfirmed PRs awaiting confirmatory response assessments. **Patients with CNS target lesions at baseline. Chemo—platinum-doublet chemotherapy; ICI—immune checkpoint inhibitors (anti-PD-1/PD-L1); MKI—multikinase inhibitors.

Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics (PK) and Efficacy of AMG 510, a Novel Small Molecule KRAS^{G12C} Inhibitor, in Advanced Solid Tumors

Marwan G Fakih, MD;[1] Bert Howard O'Neil, MD;[2] Timothy J Price, MBBS, FRACP;[3] Gerald S Falchook, MD;[5] Jayesh Desai, MBBS, FRACP;[6] James Kuo, MBBS, FRACP;[7] Ramaswamy Govindan, MD;[8] Erik Rasmussen, MS;[4] Phuong Khanh Morrow, MD;[4] Jude Ngang, PharmD;[4] Haby Henary, MD;[4] David Hong, MD[9]

[1]City of Hope, Duarte, CA, USA; [2]Indiana University, Simon Cancer Center, Indianapolis, IN, USA; [3]The Queen Elizabeth Hospital, Woodville South, AU; [4]Amgen Inc, Thousand Oaks, CA, USA; [5]Sarah Cannon Research Institute, Denver, CO, USA; [6]Peter MacCallum Cancer Centre, Melbourne, AU; [7]Scientia Clinical Research, Randwick, AU, [8]Washington University, St Louis, MO, USA; [9]MD Anderson Cancer Center, Houston, TX, USA

NSCLC: Best Tumor Response* (n=10)



IASLC 2019 World Conference on Lung Cancer UPDATE

N = 23

DCR = 96% PR 11/23 (48%); SD 11/23; PD 1/23

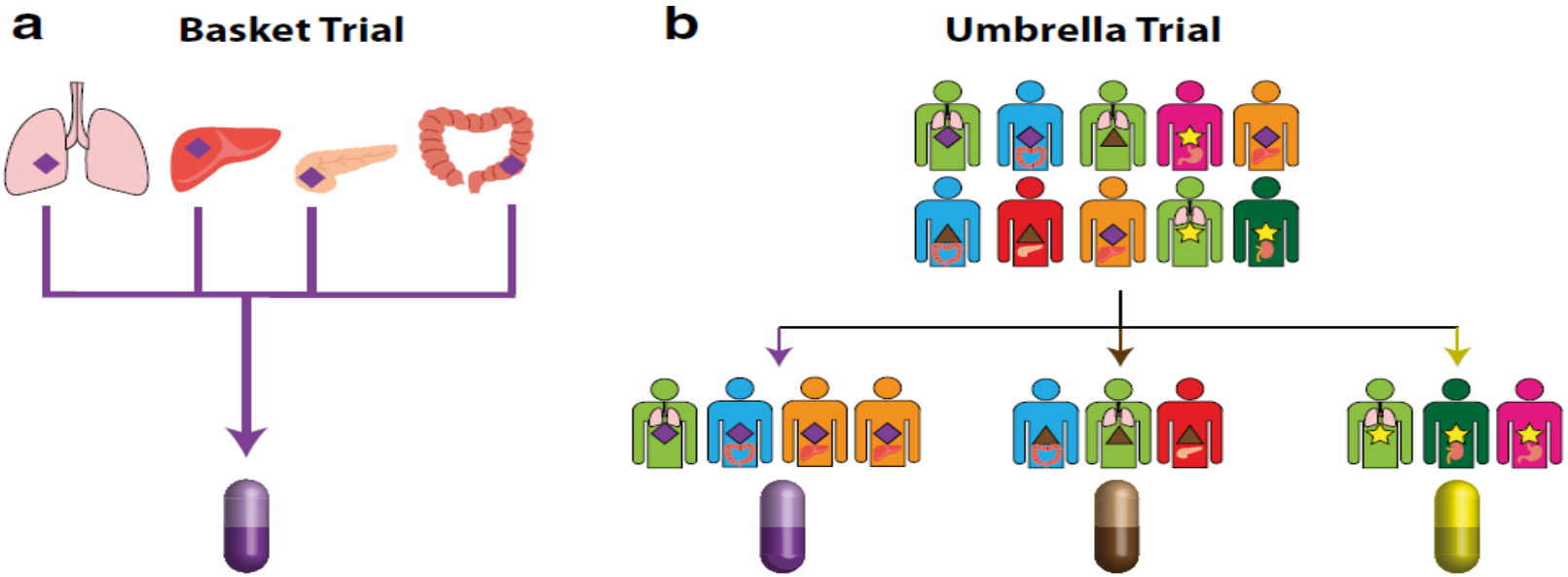
RP2D N = 13

PR 7/13 (54%); SD 6/13

Govindan et al. Abstract OA.02.02

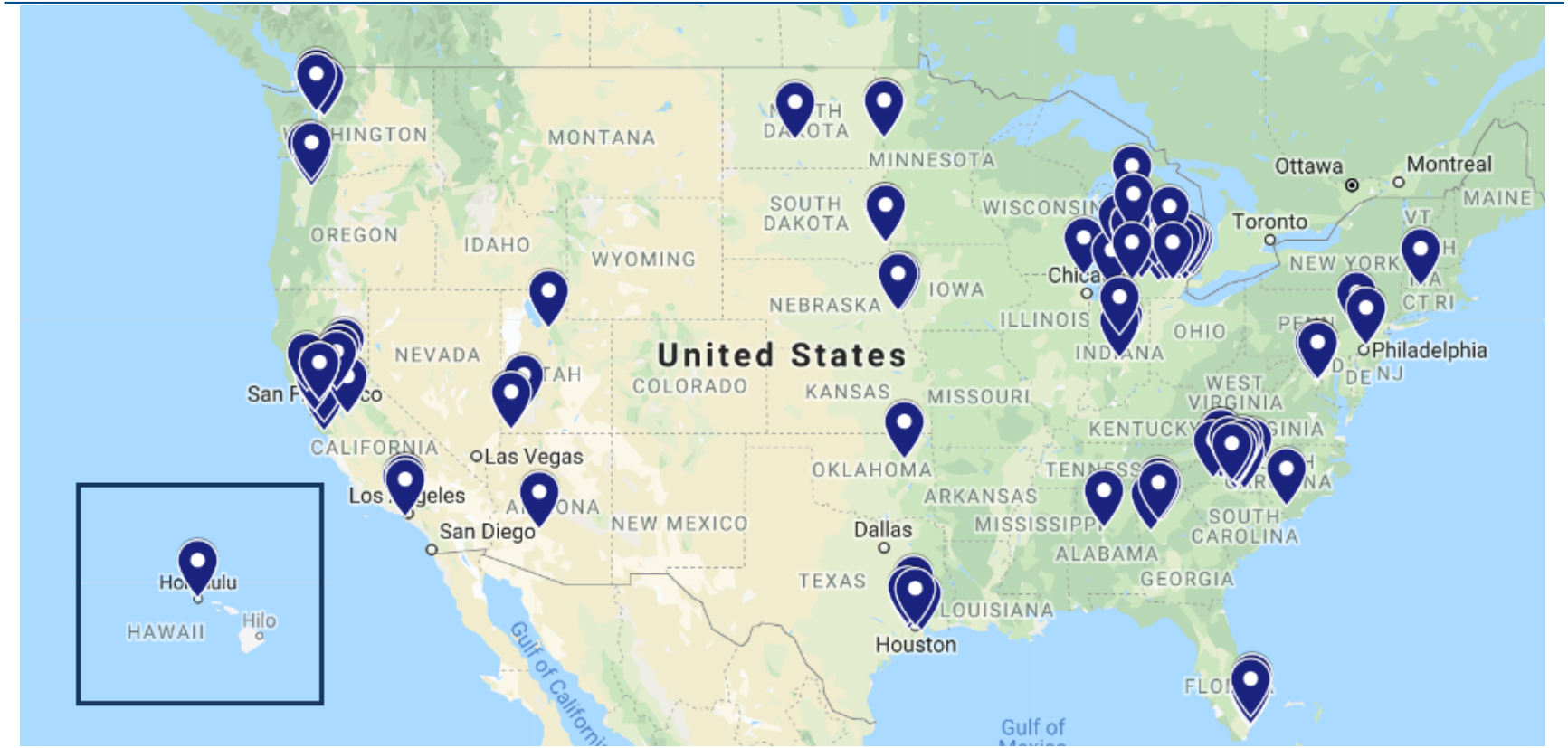
* Based on local radiographic scans every 6 weeks using RECIST 1.1 criteria
1 patient had clinical progression prior to week 6 and is not on this graph
Confirmed response
‡ 2 additional patients had confirmed PR post data cutoff
§Patient had a CR of the target lesions at week 18, post data cutoff

NEXT GENERATION GENOMIC TRIAL DESIGNS



Bui and Kummar J Mol Med 2018;96:31-38

ASCO TAPUR TRIAL: 120 LOCATIONS, 22 STATES



SARAH CANNON
Research Institute

1621 Patients Enrolled (9/16/19)

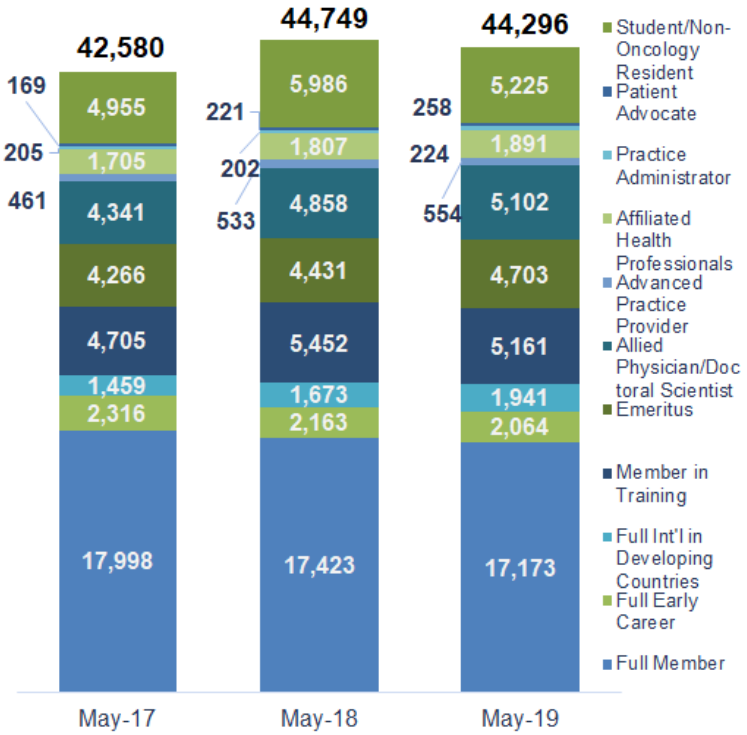
TAPUR STUDY ARM UPDATES

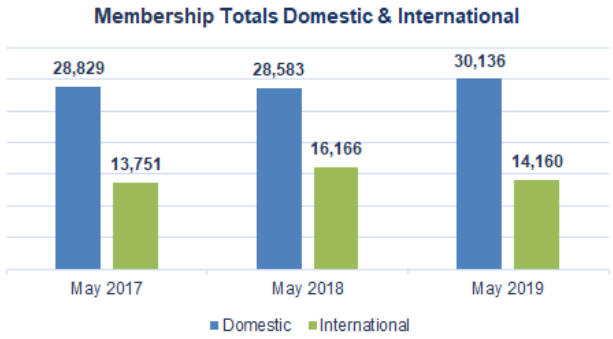
DRUG	TUMOR TYPE	VARIANT	SIGNAL
Palbociclib	Gallbladder/biliary	CDKN2A mutation/loss	
Palbociclib	Pancreas	CDKN2A mutation/loss	
Cetuximab	Breast	KRAS,NRAS, BRAF wt	
Cetuximab	NSCLC	KRAS,NRAS, BRAF wt	
Sunitinib	Colorectal	FLT3 mutation/amp	
Palbociclib	NSCLC	CDKN2A mutation/loss	
Pembrolizumab	Breast/Colorectal	High TMB	
Pertuzumab + Trastuzumab	Colorectal	ERBB2 amplification	
Vemurafenib + Cobimetinib	Colorectal	BRAF V600E/D/K/R mut	

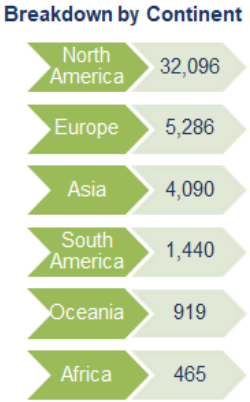
WHO BENEFITS IF THE TAPUR TRIAL SUCCEEDS?

- **Patients** receive targeted agent matched to tumor genomic profile; drugs at no cost
- **Physicians** receive guidance in interpretation of genomic test results and treatment options, access to drugs, clinical data on off-label use
- **Pharma** receives data on drug use and outcomes to inform R&D plans and life cycle management
- **Payers** receive data on test and drug use and outcomes to inform future coverage decisions
- **Regulators** receive data on extent and outcomes of off label drug and test use and real world safety data

ASCO's Membership Is Stable & Global







ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

2019 Meeting Data

Attendance

2019 AM Registration Report	2019	2018	2017
Total Attendees	> 42000	39401	38004
Professional Attendees	> 34000	32011	31023

Abstracts

- 6,205 submissions
- 3,046 International/3,159 Domestic (49%/51%)
- 2,450 accepted: (260 oral, 2190 poster +/- discussion)
- 3,265 online publication only

Video Credit: ASCO Staff Leader Mandy Davis Aiken

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Opening Session: Educate and Connect

"[To our patients]...thank you for giving us the honour of sharing a very difficult process...thank you for being our greatest teachers."

Edmond Ang, MBBCh, MRCP tells the incredible story of Chemoboy and the patients who inspire him.

At the @ASCO #OpeningSession #ASCO19

Photo Credit: Meeting Attendee

OM Ezeoke
@OME_ResidentMD

Highlight of the day was hearing @Atul_Gawande stress the importance of asking patients what their #goals are. It's of the utmost importance in oncology!

#ASCO19
#compassionatecare

Photo Credit: Meeting Attendee

Angela Saver
@a_saver

ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Affordable Care Act Medicaid Expansion Impact on Racial Disparities in Time to Cancer Treatment

Blythe Adamson[1]; Aaron Cohen[1]; Melissa Estévez[1]; Kelly Magee[1]; Erin Williams[1]; Cary Gross[2]; Neal Meropol[1]; Amy Davidoff[2]

[1] Flatiron Health, Inc. | [2] Yale University

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Amy J. Davidoff, PhD. Amy.davidoff@yale.edu

ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Presented By Blythe Adamson at 2019 ASCO Annual Meeting

OVERALL SURVIVAL (OS) RESULTS OF A PHASE III RANDOMIZED TRIAL OF STANDARD OF CARE THERAPY WITH OR WITHOUT ENZALUTAMIDE FOR METASTATIC HORMONE SENSITIVE PROSTATE CANCER (mHSPC)

ENZAMET (ANZUP 1304): AN ANZUP-LED INTERNATIONAL CO-OPERATIVE GROUP TRIAL (NHMRC CTC, CCTG, CTI, DFCI)

Christopher Sweeney, Andrew Martin, Robert Zielinski, Alastair Thomson, Thean Hsiang Tan, Shahneen Sandhu, M. Neil Reaume, David Pook, Francis Parnis, Scott North, Gavin Marx, John McCaffrey, Ray McDermott, Nicola Lawrence, Lisa Horvath, Mark Frydenberg, Simon Chowdhury, Kim Chi, Martin Stockler, Ian Davis

ANZUP® Cancer Trials Group Limited

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Christopher Sweeney, MBBS

ANNOUNCE: A randomized, placebo-controlled, double-blind, phase 3 trial of doxorubicin + olaratumab vs doxorubicin + placebo in patients with advanced soft tissue sarcomas

William D. Tap, Andrew J. Wagner, Zsuzsanna Papai, Kristen Ganjoo, Chueh-Chan Yen, Patrick Schöffski, Albiruni Razak, Javier Martin Broto, Alexander Spira, Akira Kawai, Anders Krarup-Hansen, Axel Le Cesne, Brian A. Van Tine, Yoichi Naito, Se Hoon Park, Victoria Soldatenkova, Gary Mo, Ashwin Shahir, Jennifer Wright, Robin L. Jones

On behalf of the ANNOUNCE investigators

Presented By William Tap at 2019 ASCO Annual Meeting

Olaparib as maintenance treatment following first-line platinum-based chemotherapy in patients with a germline BRCA mutation and metastatic pancreatic cancer: Phase III POLO trial

Hedy L Kindler,[1] Pascal Hammel,[2] Michele Reni,[3] Eric Van Cutsem,[4] Teresa Macarulla,[5] Michael J Hall,[6] Joon Oh Park,[7] Daniel Hochhauser,[8] Dirk Arnold,[9] Do-Youn Oh,[10] Anke Reinacher-Schick,[11] Giampaolo Tortora,[12] Hana Algül,[13] Eileen M O'Reilly,[14] David McGuinness,[15] Karen Y Cui,[16] Katia Schlienger,[17] Gershon Y Locker,[16] Talia Golan[18]

[1]The University of Chicago, Chicago, IL, USA; [2]Hôpital Beaujon (AP-HP), Clichy and University Paris VII, Paris, France; [3]IRCCS Ospedale, San Raffaele Scientific Institute, Milan, Italy; [4]University Hospitals Gasthuisberg and KU Leuven, Leuven, Belgium; [5]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [6]Fox Chase Cancer Center, Philadelphia, PA, USA; [7]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [8]University College London Cancer Institute, London, UK; [9]Asklepios Tumorzentrum Hamburg AK Altona, Hamburg, Germany; [10]Seoul National University Hospital, Seoul, South Korea; [11]St Josef-Hospital, Ruhr University Bochum, Bochum, Germany; [12]Azienda Ospedaliera Universitaria Integrata Verona, Verona and Fondazione Policlinico Universitario Gemelli IRCCS, Rome, Italy; [13]Klinikum Rechts der Isar, Department of Internal Medicine II, Technische Universität München, Munich, Germany; [14]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [15]AstraZeneca, Cambridge, UK; [16]AstraZeneca, Gaithersburg, MD, USA; [17]Merck & Co, Inc, Kenilworth, NJ, USA; [18]The Oncology Institute, Sheba Medical Center at Tel-Hashomer, Tel Aviv University, Tel Aviv, Israel

ClinicalTrials.gov identifier: NCT02184195. This study was sponsored by AstraZeneca and is part of an alliance between AstraZeneca and Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA (MSD)

Presented By Hedy Kindler at 2019 ASCO Annual Meeting

FDA-CLQ AM19 Abstracts - Oral Presentations

1. Impact of broadening clinical trial eligibility criteria for advanced non-small cell lung cancer patients: Real-world analysis

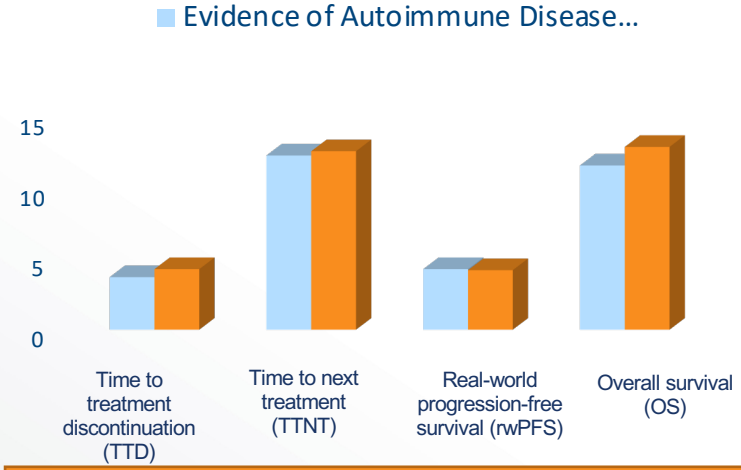
Harvey et al., ASCO Annual Meeting 2019, Abstract # LBA108

Original Cohort	10,500 (100%)
Traditional Exclusions	
Pts excluded for brain mets	2,226 (21.2%)
Pts excluded for prior/concurrent malignancy	2,254 (21.5%)
Pts excluded for CrCl < 60 mL/min	1,509 (14.4%)
Total pts included by traditional criteria	5,495 (52.3%)
Pts excluded by 1 of 3 traditional criteria	**5,005 (47.7%)**
Expanded Criteria (Permits brain mets and prior/concurrent malignancy)	

Using expanded clinical trial eligibility criteria would enable ~2x # of advanced NSCLC pts to consider trial participation

2. Real-world outcomes of patients w/ advanced NSCLC receiving immune checkpoint inhibitors w/ and w/o autoimmune disease (AD)

Khozin et al., ASCO Annual Meeting 2019, Abstract # 9110



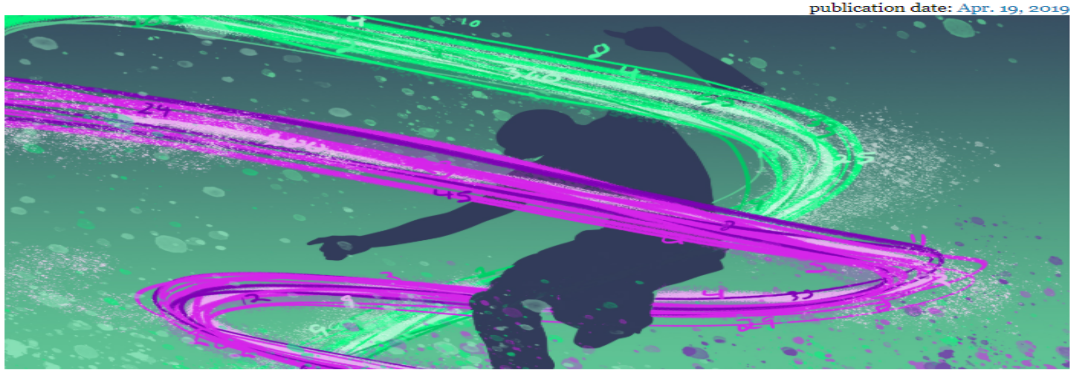
No statistical difference in outcomes in patients with and without AD

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

THE CANCER LETTER

Inside information on cancer research and drug development

publication date: Apr. 19, 2019



Real World Evidence

How FDA, Pfizer, and Flatiron Health did it

Approval of Ibrance for men affords a glance at use of real world data

By Paul Goldberg

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

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

ASCO Research Priorities Identified

- Identify strategies that better predict response to immunotherapies
- Better define the patient populations that benefit from post-operative (adjuvant) therapy
- Translate innovations in cellular therapies for hematological malignancies to solid tumors
- Increase precision medicine research and treatment approaches in pediatric cancers
- Optimize care for older adults with cancer
- Increase equitable access to cancer clinical trials
- Reduce the long-term consequences of cancer treatment
- Reduce obesity's impact on cancer incidence and outcomes
- Identify strategies to detect and treat premalignant lesions

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

UNITE AND CONQUER: ACCELERATING PROGRESS TOGETHER

Bridging Gaps and Connecting People to Find a Better Way

Scientific Program Chair
Melissa Johnson, MD
Sarah Cannon

Education Program Chair
Tatiana Prowell, MD
FDA/Johns Hopkins

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

ASCO 2020 - UNITE AND CONQUER: ACCELERATING PROGRESS TOGETHER

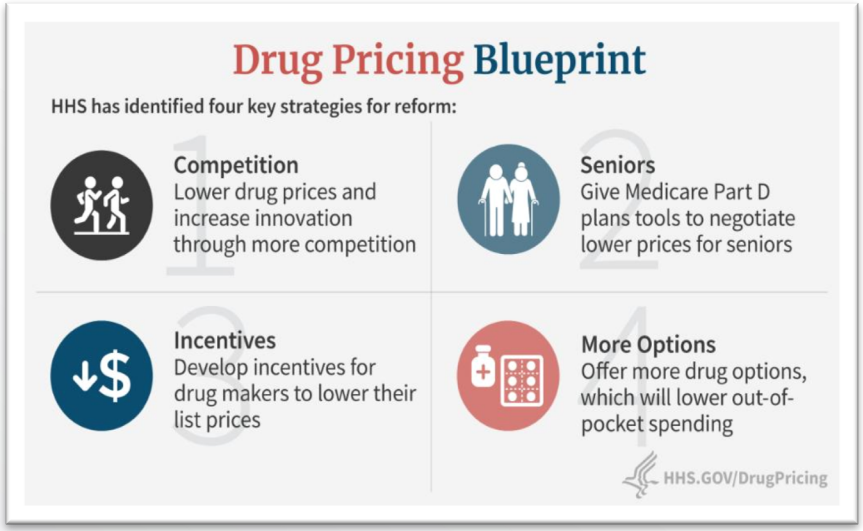
- Bringing together stakeholders
  (physicians, patients, nurses, pharma, regulators, payers, scientists)
- Leading research initiatives
  (eligibility, access, profiling, etc.)
- Expanding our membership
- Being the preeminent cancer meeting

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Drug Pricing

*"One of my greatest priorities is to **reduce the price of prescription drugs.**"*

PRESIDENT DONALD J. TRUMP



ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Congress' Potential Fall Agenda

- Healthcare:
  - Drug pricing
  - Appropriations
  - Surprise medical billing
  - E-cigarettes

- Outside healthcare:
  - Impeachment
  - Gun control
  - Trade deals
  - Surveillance issues
  - National Defense Authorization Act

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

What ASCO Has Supported

- **Price Transparency:** Allowing greater transparency on all aspects of drug pricing
- **Pay for delay/evergreening/product hopping:** Preventing manufacturers from participating in anti-competitive behaviors
- **Reducing Market Exclusivity**: Reducing the time it takes before a generic/biosimilar can enter the market
- **Patient Out of Pocket Maximums in Part D**

ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Where ASCO Has Raised Concerns

- Policy changes that could negatively impact cancer patients and Medicare Part B drug reimbursement:
  - Including value of coupons in the determination of Average Sales Price
  - Establishing a Maximum Add-on Payment for Part B drugs

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

SARAH CANNON
Research Institute

THANK YOU