2018 - 2019
WHAT'S NEW IN CANCER CARE?
ADVANCES IN DIAGNOSIS AND TREATMENT

FCDS ANNUAL CONFERENCE

ORLANDO, FLORIDA

8/1/2019

STEVEN PEACE, CTR

CDC & FLORIDA DOH ATTRIBUTION

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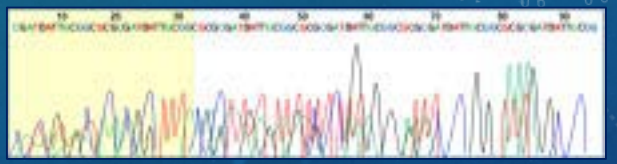
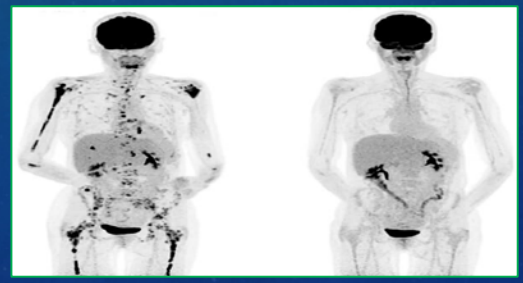
PRESENTATION OUTLINE

- Introduction
- 2019 Incidence & Mortality Estimates
- AACR Cancer Progress Report 2018
- FDA Novel Drug Approvals in 2018
- ASCO 2019 Clinical Cancer Advances
- NCCN Annual Report 2018
- 2019 Annual Report to the Nation on the Status of Cancer
- Update on National Cancer Moonshot Initiative
- NCI Match Trial - Mutations and Agents
- Molecular Testing for Solid Tumors 2019
- Questions



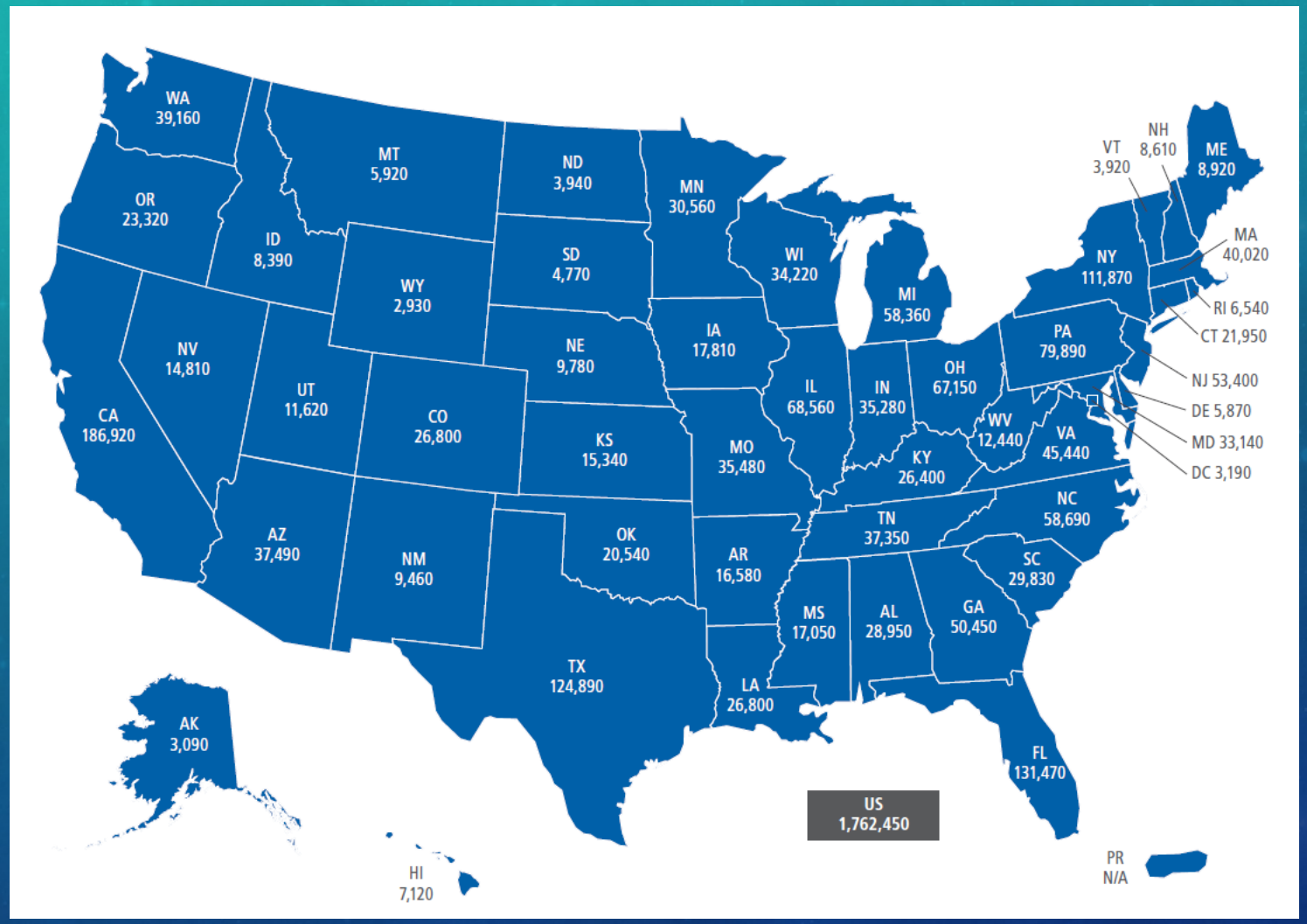


INTRODUCTION

- In 2018, the US Food and Drug Administration (FDA) approved a record 59 new drugs across all medical specialties; of these, 17 (29%) approvals were relevant to oncology/hematology specifically.
- This represents an increase from 2017, in which the FDA approved 12 new oncology/hematology agents.
- 8 of the 17 oncology/hematology approvals in 2018 are indicated for the treatment of various blood cancers.
- Breast - the risk of invasive recurrence of human epidermal growth factor receptor 2–positive, early-stage breast cancer was 50% lower in patients treated with ado-trastuzumab emtansine compared with those who received trastuzumab alone. This finding supports the use of ado-trastuzumab emtansine as a new standard of care in these patients.
- Two CLL [chronic lymphocytic leukemia] studies established ibrutinib as the standard of care for front-line treatment of CLL in the younger and older populations, respectively.
- Adenocarcinoma of Lung - Paz-Ares et al found that adding pembrolizumab to chemotherapy (pemetrexed and carboplatin) nearly doubled the objective response rate (ORR) in patients and is in tolerable safety profile.
- Lung – Target Therapy - New EGFR inhibitor delays lung cancer progression in drug resistant mutations of EGFR – osimertinib (Tagrisso)
- Prostate - two new agents for treatment of high-risk, non-metastatic, castration-resistant prostate cancer was particularly important. Apalutamide and enzalutamide approved by the FDA based on findings of SPARTAN and PROSPER trials.
- Immunotherapy - Nobel Prize in Physiology or Medicine awarded to James P. Allison of United States and Tasuku Honjo of Japan for work on cancer immunotherapy. Their findings on checkpoint inhibitors “brought immunotherapy out from decades of skepticism.”
- Combination Immunotherapy - Combination of two immunotherapy agents, nivolumab and ipilimumab in patients with intermediate or high-risk RCC improved 18-month overall survival compared with tyrosine kinase inhibitor sunitinib (Sutent), 75% for the combination *v* 60% for sunitinib. And, 9% of patients receiving nivolumab with ipilimumab had complete regression of the cancer.
- Radiation Therapy - SBRT [stereotactic body radiation therapy] for the treatment of oligometastatic disease (small number of mets)

http://www.cancernetwork.com/oncology-journal/key-advances-oncology-2018

2019 INCIDENCE & MORTALITY ESTIMATES



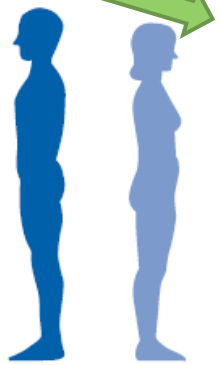
2018 Cancer Facts and Figures – American Cancer Sociery

2019 INCIDENCE & MORTALITY ESTIMATES

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2019 Estimates

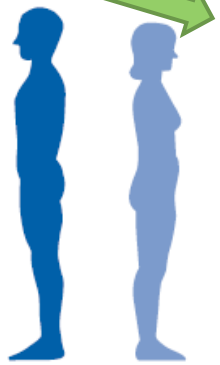
Estimated New Cases

Male			Female		
Prostate	174,650	20%	Breast	268,600	30%
Lung & bronchus	116,440	13%	Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%	Colon & rectum	67,100	7%
Urinary bladder	61,700	7%	Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%	Melanoma of the skin	39,260	5%
Kidney & renal pelvis	44,120	5%	Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%	Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%	Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%	Pancreas	26,830	3%
Pancreas	29,940	3%	Leukemia	25,860	3%
All sites	870,970		All sites	891,480	



Estimated Deaths

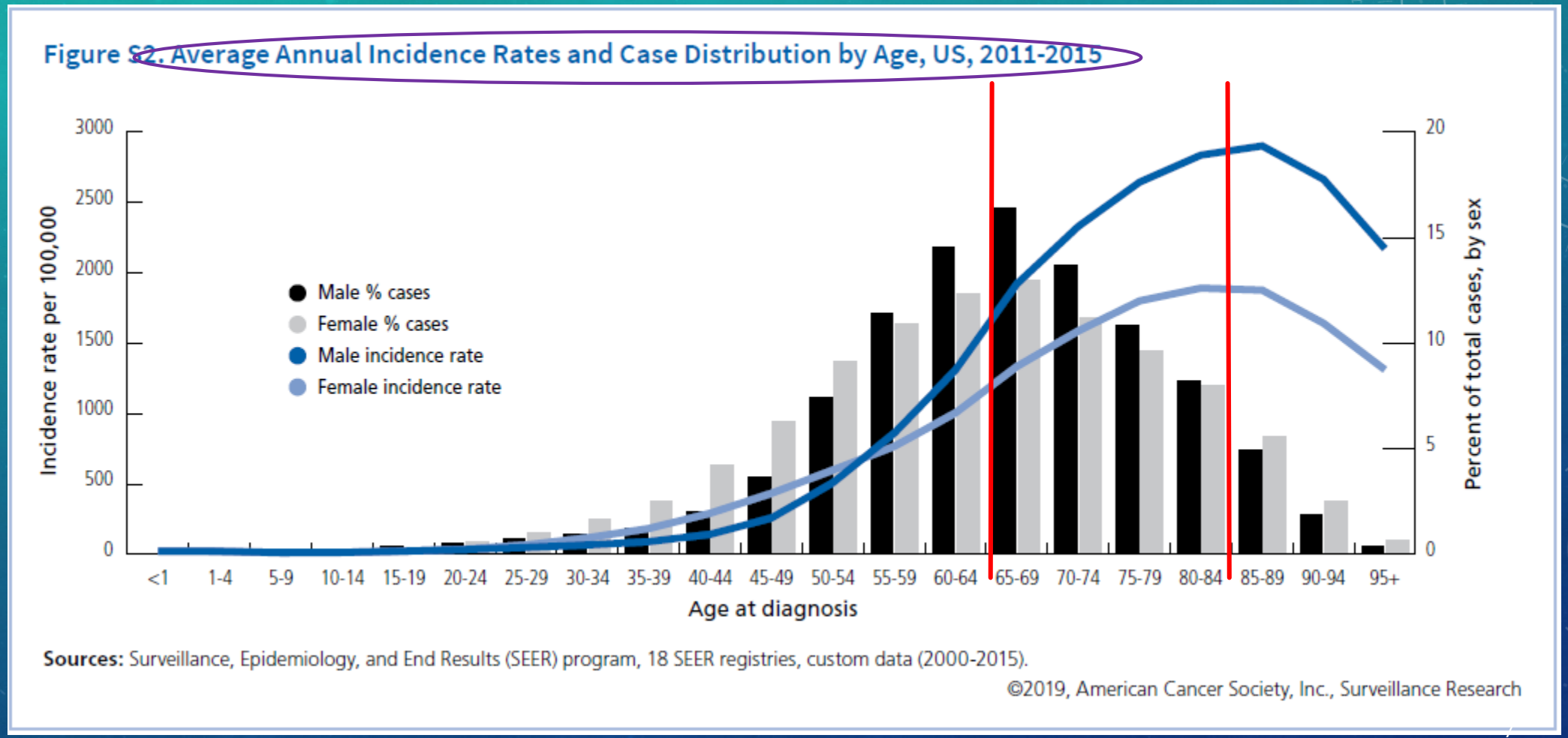
Male			Female		
Lung & bronchus	76,650	24%	Lung & bronchus	66,020	23%
Prostate	31,620	10%	Breast	41,760	15%
Colon & rectum	27,640	9%	Colon & rectum	23,380	8%
Pancreas	23,800	7%	Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%	Ovary	13,980	5%
Leukemia	13,150	4%	Uterine corpus	12,160	4%
Esophagus	13,020	4%	Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%	Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%	Brain & other nervous system	7,850	3%
All sites	321,670		All sites	285,210	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

2018 Cancer Facts and Figures – American Cancer Society

2019 INCIDENCE & MORTALITY ESTIMATES



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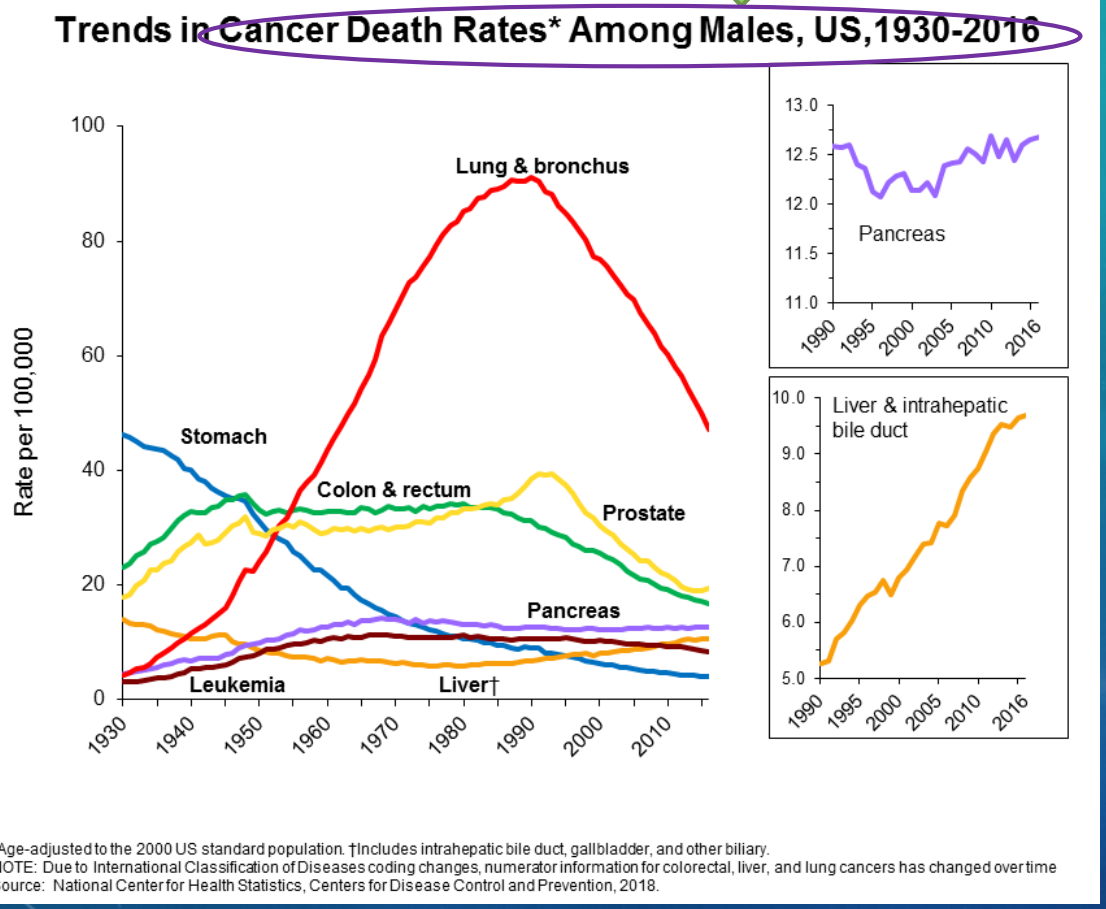
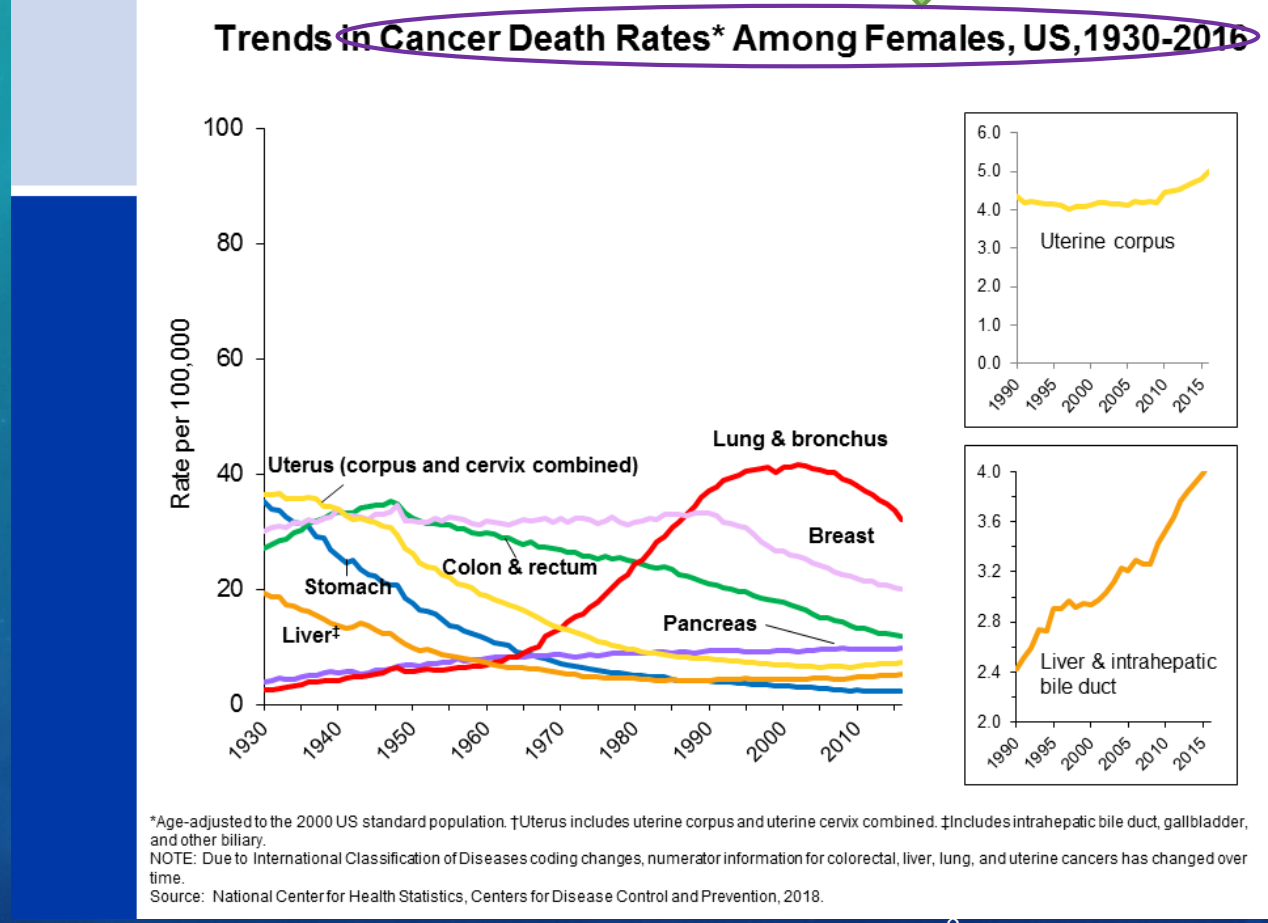
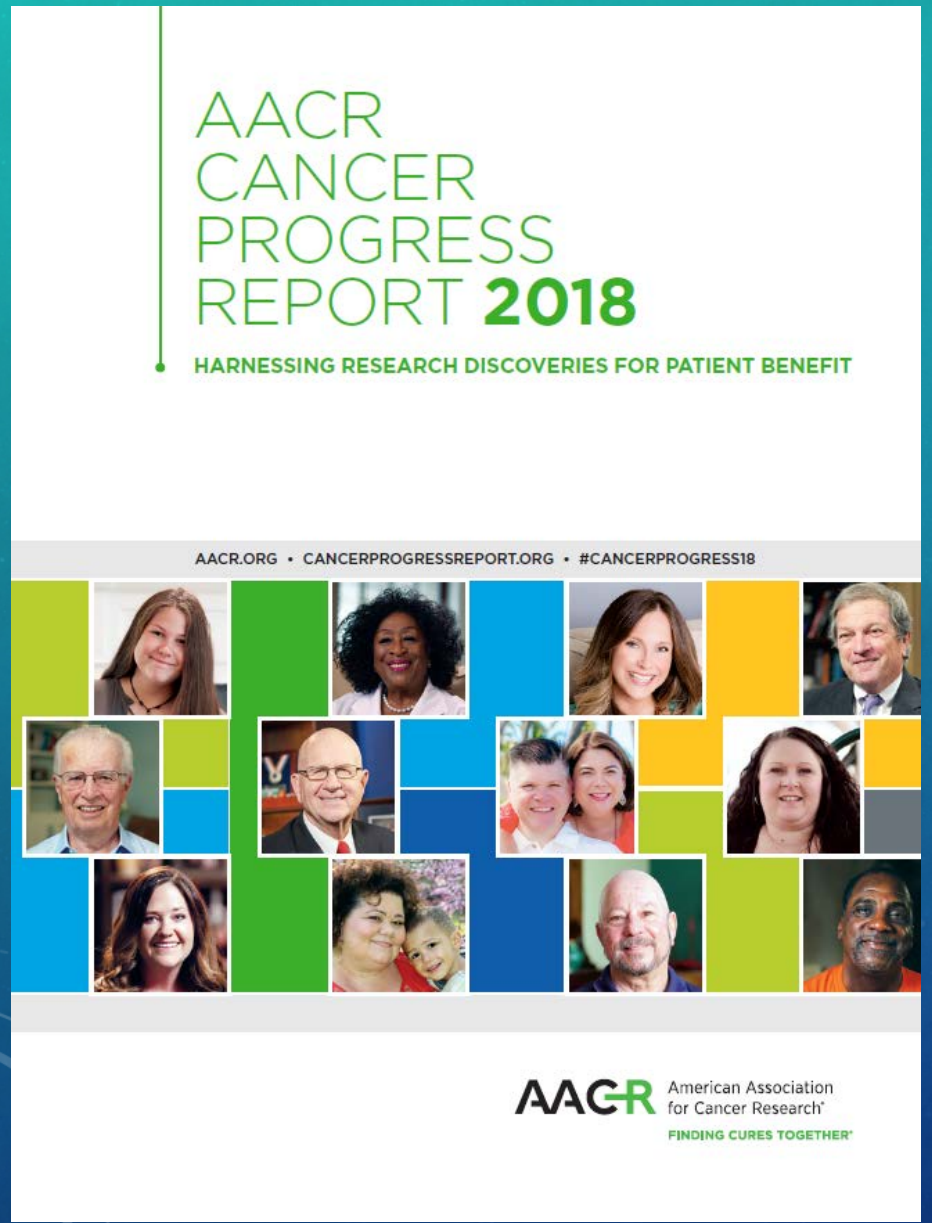




2018 Cancer Facts and Figures – American Cancer Sociery

AACR CANCER PROGRESS REPORT 2018



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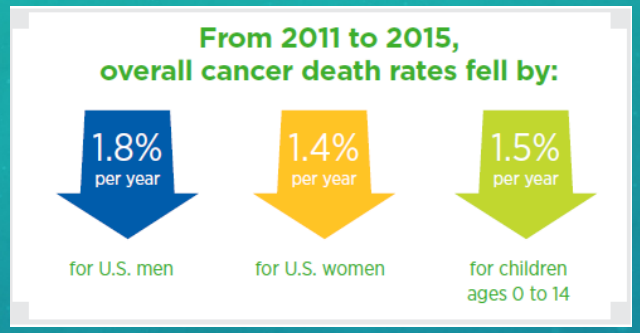
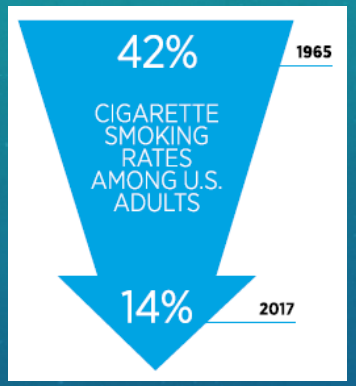
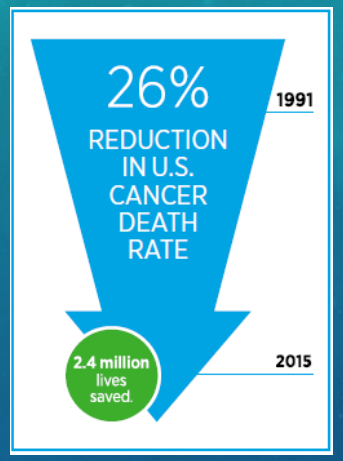
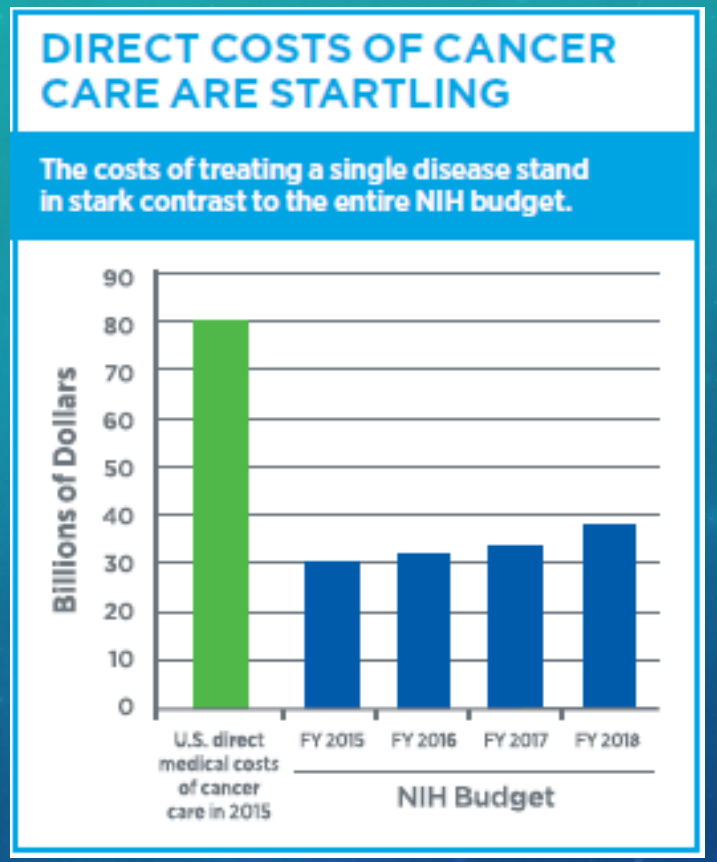
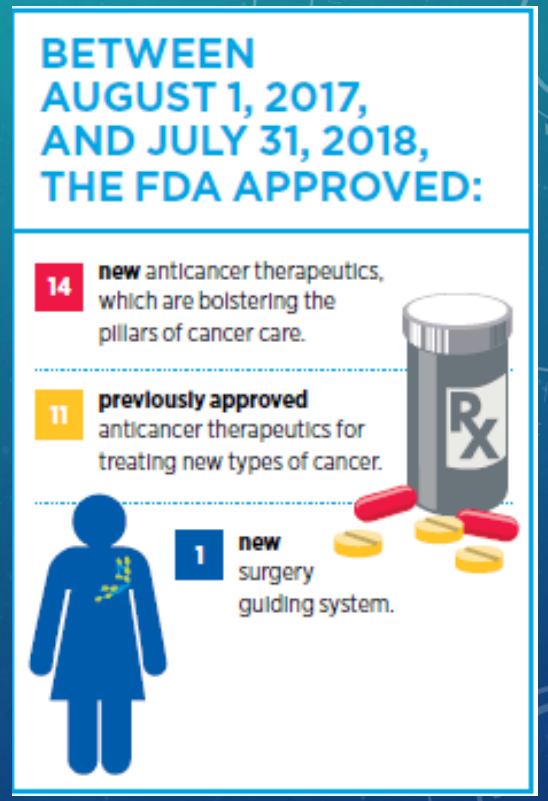
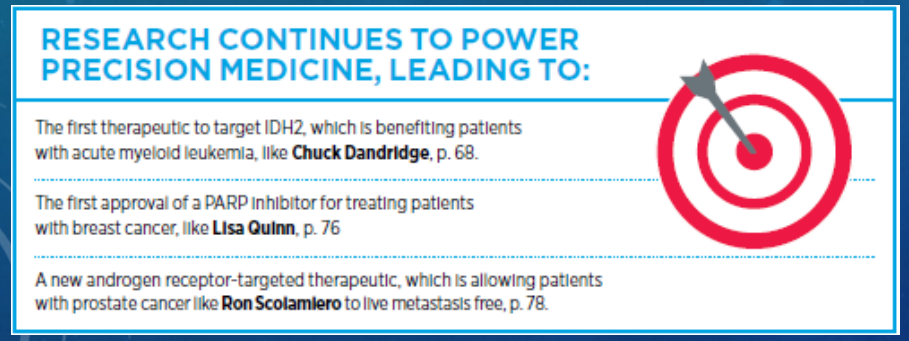


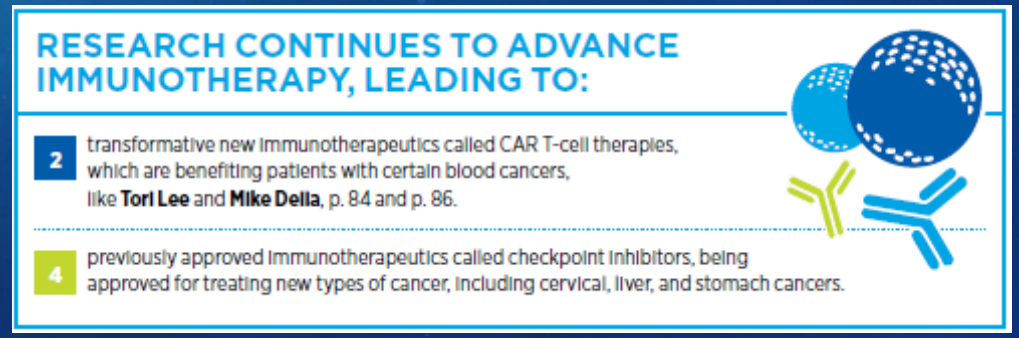












AACR CANCER PROGRESS REPORT 2018

TABLE 1 NEWLY FDA-APPROVED ANTICANCER THERAPEUTICS: AUGUST 1, 2017–JULY 31, 2018

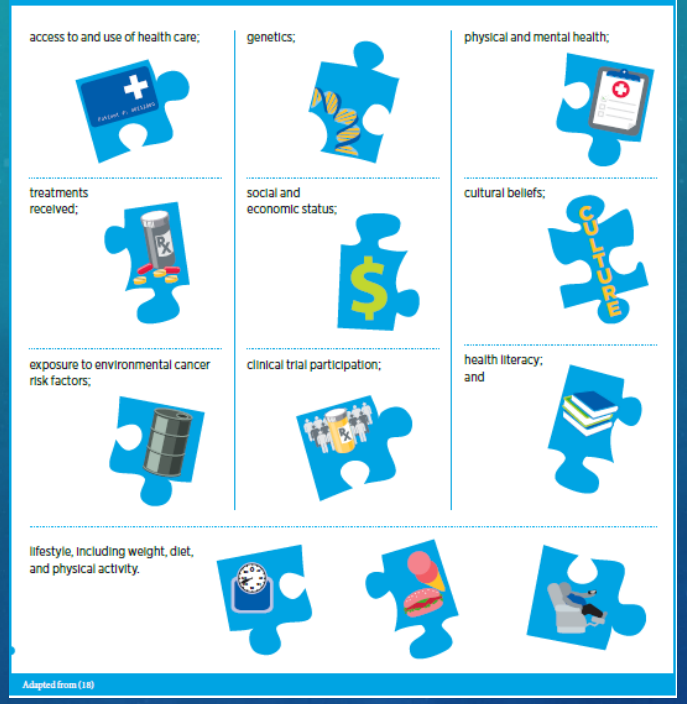
Approved Indication	Generic Name	Trade Name	Formulation
CAR T-cell Therapy			
Certain type of non-Hodgkin lymphoma	axicabtagene ciloleucel	Yescarta	IV
Certain types of leukemia and non-Hodgkin lymphoma†	tisagenlecleucel	Kymriah	IV
Cell-cytoskeleton Modifying Agents			
Certain type of non-Hodgkin lymphoma†	brentuximab vedotin	Adcetris	IV
Cell-signaling Inhibitors			
Certain type of breast cancer	abemaciclib	Verzenio	Oral
Certain type of non-Hodgkin lymphoma	acalabrutinib	Calquence	Oral
Certain type of non-Hodgkin lymphoma	copanlisib	Aliqopa	IV
Certain type of thyriod cancer†	dabrafenib and trametinib	Tafinlar and Mekinist	Oral + Oral
Certain type of melanoma	encorafenib and binimetinib*	Braftovi and Mektovi	Oral + Oral
Certain type of blood cancer†	vemurafenib	Zelboraf	Oral
DNA-damaging Agents			
Certain types of leukemia	daunorubicin and cytarabine	Vyxeos	IV
Certain types of leukemia	inotuzumab ozogamicin	Besponza	IV
Certain type of leukemia†	gemtuzumab ozogamicin	Mylotarg	IV
DNA-repair Inhibitors			
Certain breast cancers†	olaparib*	Lynparza	Oral
Epigenome-modifying Agents			
Certain type of leukemia	enasidenib*	Idhifa	Oral
Certain type of leukemia	ivosidenib*	Tibsovo	Oral
Hormones/Antihormones			
Prostate cancer	apalutamide	Erleada	Oral
Immune-checkpoint Inhibitors			
Certain type of lung cancer†	durvalumab	Imfinzi	IV
Certain types of colorectal† and liver cancer†	nivolumab	Opdivo	IV
Certain types of colorectal and kidney cancer†	nivolumab and ipilimumab	Opdivo and Yervoy	IV + IV
Certain types of lymphoma, stomach, and cervical cancer†	pembrolizumab*	Keytruda	IV
Radiation-emitting Therapeutics			
Certain types of neuroendocrine tumors	lutetium 177 dotatate	Lutathera	IV
Certain types of neuroendocrine tumors	iobenguane I 131	Azedra	IV

†new cancer type approved 2017–2018
* requires a companion diagnostic

Where multiple trade names are used, only the most common have been listed

WHY DO CANCER HEALTH DISPARITIES EXIST?

Complex and interrelated factors contribute to U.S. cancer health disparities. The factors may include, but are not limited to, differences and/or inequalities in:



Adapted from (18)

U.S. CANCER HEALTH DISPARITIES

Significant progress has been made against cancer. However, not everyone has benefited equally from the advances and adverse differences in numerous cancer measures exist among certain segments of the U.S. population (see sidebar on What Are Cancer Health Disparities? p. 12). Some recently identified examples of disparities in cancer incidence rates, death rates, and stage at diagnosis are highlighted here. Disparities in other cancer measures are outlined elsewhere in the report (see sidebars on Disparities in the Burden of Avoidable Cancer Risk Factors, p. 26; Disparities in Cancer Screening, p. 47; Disparities in Cancer Clinical Trial Participation, p. 51; Disparities in Treatment, p. 57; and Disparities in Quality of Life after a Cancer Diagnosis, p. 96).

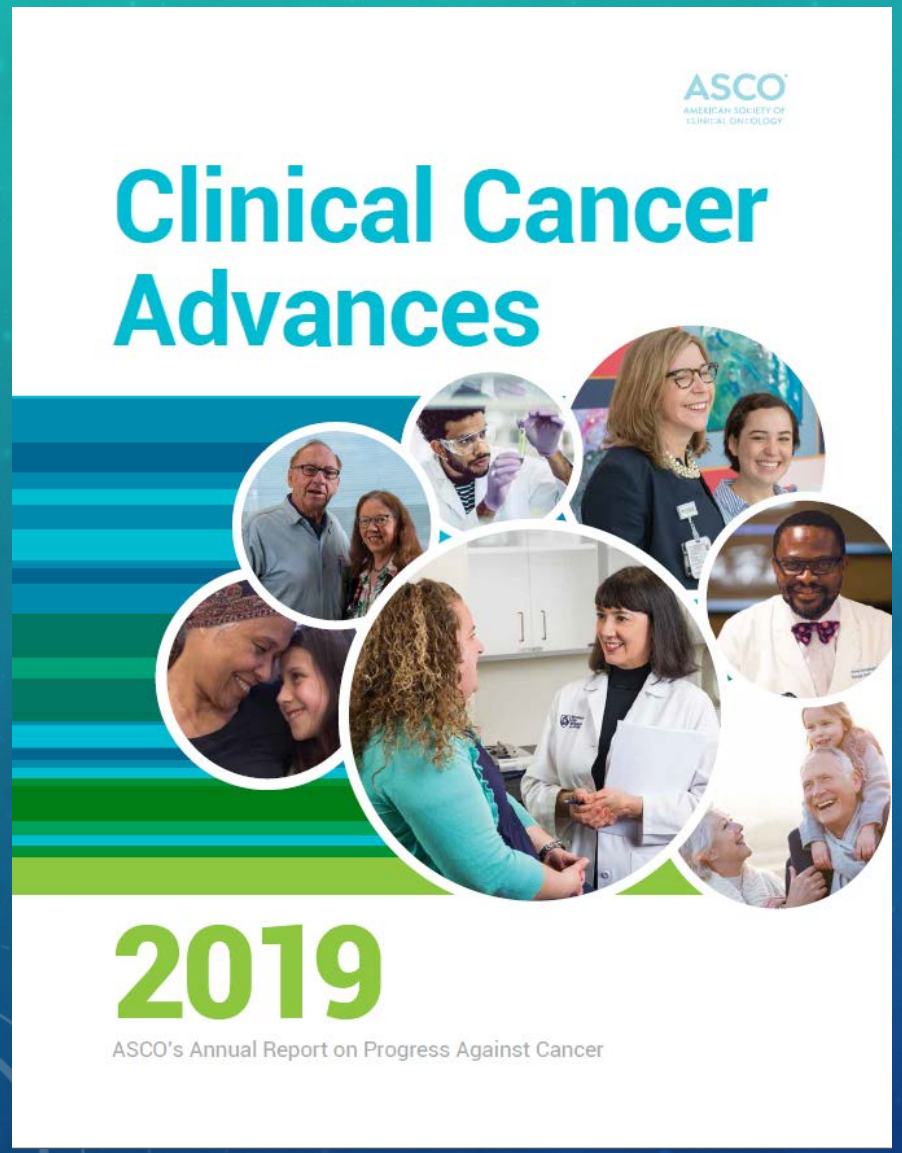
MORE THAN **DOUBLE**	Non-Hispanic black men have a prostate cancer death rate that is **more than double** that for men in any other racial or ethnic group (2).
75% AND 69% MORE LIKELY	African-American and Hispanic women are **75 percent and 69 percent**, respectively, **more likely** to be diagnosed with breast cancer at an advanced stage than non-Hispanic white women (12).
DOUBLE	Non-Hispanic black women have a triple-negative breast cancer incidence rate that is **double** that for non-Hispanic white women (13).
39% HIGHER	Non-Hispanic black women have a breast cancer death rate that is **39 percent higher** than that for non-Hispanic white women (13).
26% HIGHER	Men living in Appalachia have a lung cancer incidence rate that is **26 percent higher** than that for men living in the remainder of the United States (14).
61% AND 51% MORE LIKELY	Adolescents and young adults (ages 15 to 39) with head and neck cancer who have Medicaid coverage or no insurance are **61 percent and 51 percent**, respectively, **more likely** to die from their disease than those who have private insurance (15).
MORE THAN **20%** MORE LIKELY	Patients of low socioeconomic status with anal cancer are **more than 20 percent more likely** to die from the disease than those of high socioeconomic status (16).
3X MORE LIKELY	Women living with a same-sex relationship partner are **three times more likely** to die from breast cancer than women living with a male spouse or cohabiting relationship partner (17).

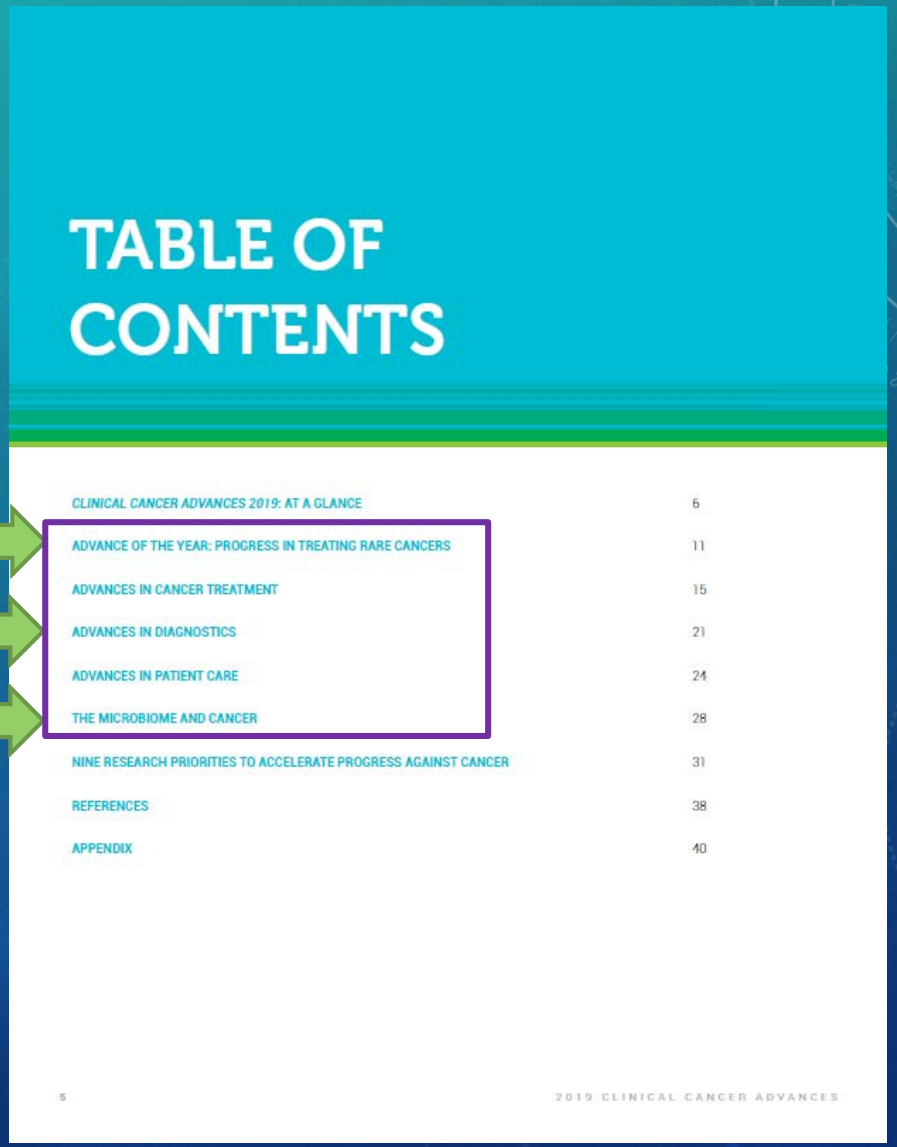
FDA NOVEL DRUG APPROVALS FOR 2018

Drug Name	Active Ingredient	FDA-Approved Use
Elzonris	Tagraxofusp-erzs	Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDC)
Asparlas	Calaspargase pegol-mknl	acute lymphoblastic leukemia (ALL) in pediatric and adult patients age 1 month to 21 years
Xospata	gilteritinib	Relapsed or refractory acute myeloid leukemia (AML)
Daurismo	glasdegib	Newly-diagnosed acute myeloid leukemia (AML)
Gamifant	emapalumab-lzsg	hemophagocytic lymphohistiocytosis (HLH)
Lorbrena	lorlatinib	anapalastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer
Talzenna	talazoparib	locally advanced or metastatic breast cancer with germline BRCA mutation
Vizimpro	dacomitinib	metastatic non-small-cell lung cancer
Libtayo	cemiplimab-rwlc	cutaneous squamous cell carcinoma (CSCC)
Copiktra	duvelisib	relapsed or refractory chronic lymphocytic leukemia, lymphocitic lymphoma, follicular lymphoma
Lumoxiti	moxetumomab pasudotox-tdfk	hairy cell leukemia
Poteligeo	mogamulizumab-kpkc	two rare types of non-Hodgkin lymphoma
Tibsovo	ivosidenib	relapsed or refractor acute myeloid leukemia (AML)
Braftovi	encorafenib	unresectable or metastatic melanoma
Mektovi	binimetinib	unresectable or metastatic melanoma
Erleada	apalutamide	prostate cancer
Lutathera	lutetium Lu 177 dotatate	pancreatic and gastrointestinal tract gastroenteropancreatic neuroendocrine tumors (NETs)

2018 New Approvals Report (/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM629290.pdf)

ASCO 2019 CLINICAL CANCER ADVANCES





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ASCO 2019 CLINICAL CANCER ADVANCES

Advance of the Year: Progress in Rare Cancers

This year, ASCO names Progress in Treating Rare Cancers as the Advance of the Year. In the United States, rare cancers account for about 20% of all cancers diagnosed each year, and incidence rates vary worldwide.[4] Progress has historically lagged behind the achievements made in more common cancers; however, five major studies this past year offer significant steps forward, making this a notable year for advances in rare cancers:

1. **A new combination of targeted therapies for a rare, hard-to-treat form of thyroid cancer** produced responses in over two thirds of patients

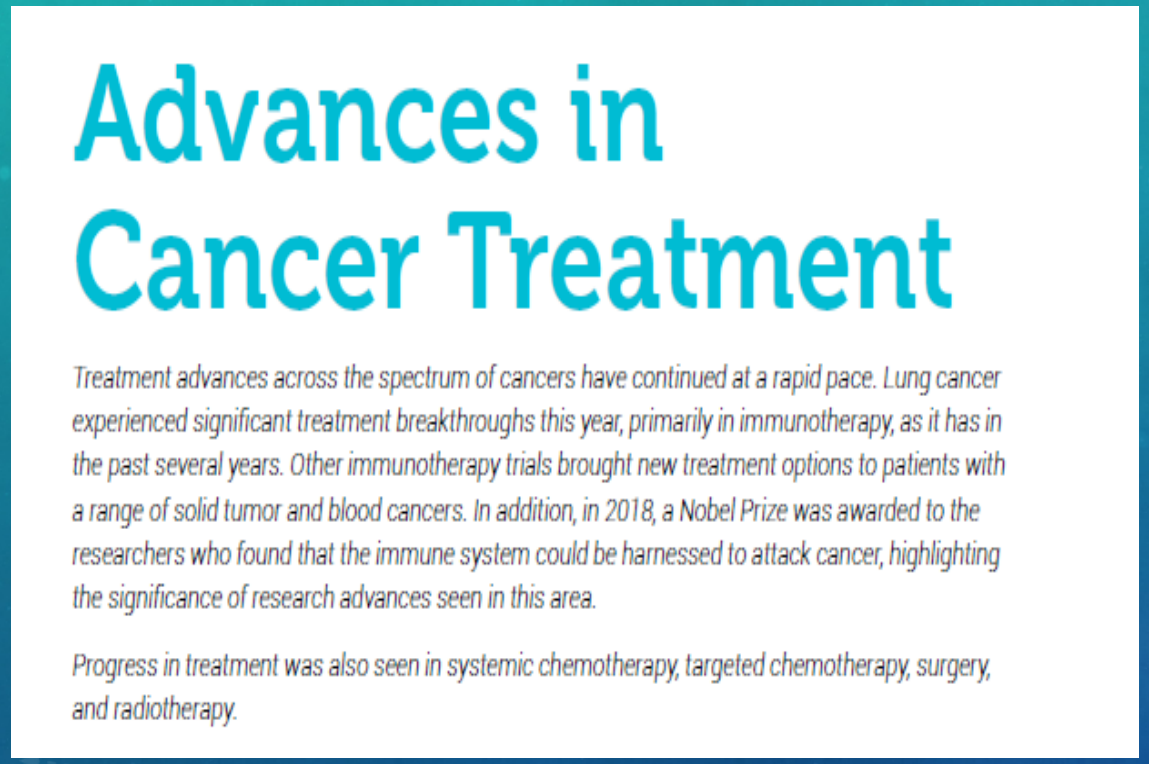
2. Sorafenib became the **first treatment to improve progression-free survival for desmoid tumors,** a rare type of sarcoma

3. Lutetium Lu 177 dotatate (^{177}Lu Dotatate), a new therapy that delivers targeted radiation to tumor cells, **lowered the risk of disease progression or death by 79% for patients with advanced midgut neuroendocrine tumors,** compared to standard treatment

4. Trastuzumab, a standard treatment for HER2 positive breast cancer, **significantly slowed progression of HER2-positive uterine serous carcinoma**

5. **The first promising therapy**—the colony stimulating factor 1 inhibitor pexidartinib—**for a rare cancer of the joints known as tenosynovial giant cell tumor, showed an overall response rate of 39.3%,** v 0% for those taking a placebo

ASCO 2019 CLINICAL CANCER ADVANCES



- Immunotherapy
  - Checkpoint Inhibitors
  - Combination Immunotherapy – melanoma, renal cell carcinoma
  - PD-1 Inhibitor for skin cancer
  - Pembrolizumab for H&N with high PD-L1
  - CAR-T therapy trials show longer term benefits
- Targeted Therapies
  - Tagrisso (EGFR Inhibitor) delays lung cancer progression
  - Verzenio (protein-targeted therapy) delays progression for CDK4/6 active advanced breast cancers
  - Vidaza and Dacogen for elderly patients with AML
- Other Therapeutic Approaches
  - Less is more for ovarian cancers – no 2nd look surgery
  - Xtandi or Erleada f+
  - or hormone resistant prostate cancer

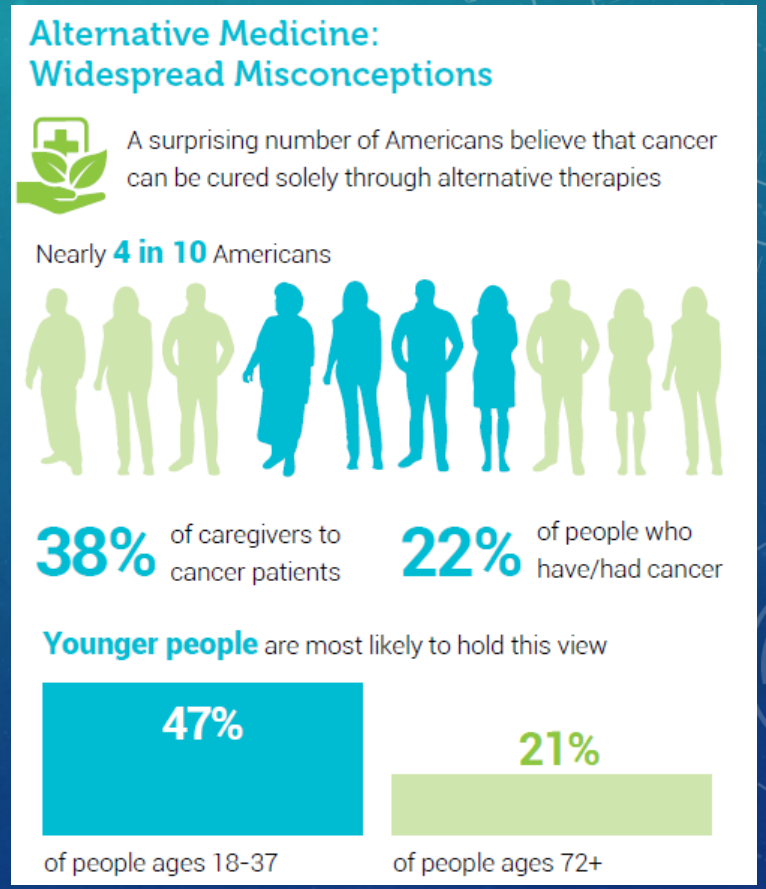
ASCO 2019 CLINICAL CANCER ADVANCES

Advances in Diagnostics

This year marked a major advance with a molecular test that can help many women with early-stage breast cancer safely forgo chemotherapy. There were also advances in the use of liquid biopsies for refining treatment in several major cancers.

- Advances in Liquid Biopsy for Early Detection using protein biomarkers and tumor-specific mutations in circulating DNA found in blood samples
- 21-gene expression assay identifies women who can safely skip adjuvant chemotherapy for HR+/HER2- breast cancer in women over age 50 with low and intermediate recurrence risk scores of 0-10 and 11-25 respectively

Not All is Good News



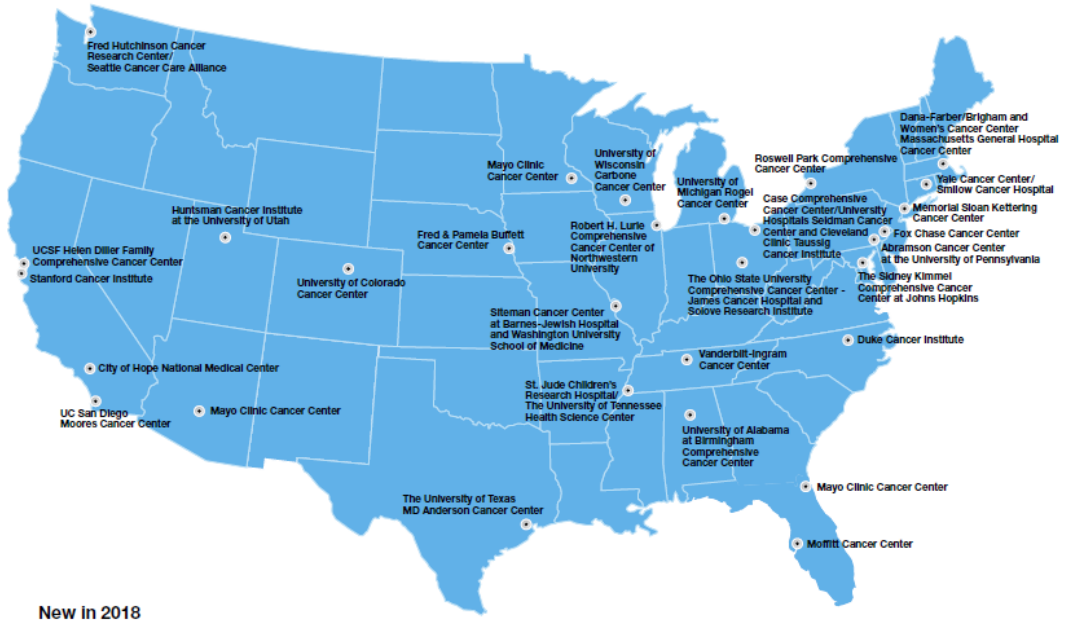
Alternative Medicine Is Not a Substitute for Conventional Therapy

NCCN ANNUAL REPORT 2018

Advancing Quality Cancer Care

2018 Annual Report

National Comprehensive Cancer Network®



New in 2018

Abramson Cancer Center at the University of Pennsylvania becomes the 28th NCCN Member Institution.

NCCN ANNUAL REPORT 2018

NCCN Guidelines

NCCN Guidelines are the most thorough and frequently updated clinical practice guidelines available in any area of medicine.

NCCN Guidelines

ABOUT

- Contain cancer care recommendations that are continuously updated and revised to reflect new data and clinical information
- NCCN Categories for Evidence and Consensus are based on the level of clinical evidence available and the degree of consensus within NCCN Guidelines Panels.
- NCCN Categories of Preference clarify panel and institutional preferences for interventions, provide guidance to users of the NCCN Guidelines on which recommendation(s) is considered optimal, and continue to provide a wide range of recommendations to meet varying clinical circumstances and patient preferences.
- NCCN Guidelines with NCCN Evidence Blocks™ are a visual representation of five key measures that provide important transparent information about specific NCCN Guidelines recommendations that informs decisions about systemic therapies based upon treatment, supporting data, and cost. It is a starting point for shared decision-making considering the patient's own value system. NCCN Evidence Blocks™ are included in 47 out of 51 NCCN Guidelines that include systemic therapies, which are free and available at NCCN.org.

TYPES

- NCCN Guidelines for Treatment of Cancer by Site apply to 97% of cancer cases in the United States
- NCCN Guidelines for Detection, Prevention, & Risk Reduction
- NCCN Guidelines for Supportive Care
- NCCN Guidelines for Specific Populations
- NCCN Guidelines with NCCN Evidence Blocks™

ACCESS

- Free download online from NCCN.org
- NCCN Mobile App
- Print copies
- Pocket Guidelines
- E-mail alerts (with subscription to NCCN Flash Updates™)
- Health Information Technology (HIT) companies

In 2018, NCCN added five NEW NCCN Guidelines:

NCCN Guidelines for Treatment of Cancer by Site

Acute Lymphoblastic Leukemia
Acute Myeloid Leukemia
AIDS-Related Kaposi Sarcoma
Anal Carcinoma
B-Cell Lymphomas
Basal Cell Skin Cancer
Bladder Cancer
Bone Cancer
Breast Cancer
Central Nervous System Cancers
Cervical Cancer
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
Chronic Myeloid Leukemia
Colon Cancer
Cutaneous Melanoma
Dermatofibrosarcoma Protuberans
Esophageal and Esophagogastric Junction Cancers
Gastric Cancer
NEW Gestational Trophoblastic Neoplasia
Hairy Cell Leukemia
Head and Neck Cancers
Hepatobiliary Cancers
Hodgkin Lymphoma
Kidney Cancer
Malignant Pleural Mesothelioma
Merkel Cell Carcinoma
Multiple Myeloma
Myelodysplastic Syndromes
Myeloproliferative Neoplasms
Neuroendocrine and Adrenal Tumors
Non-Small Cell Lung Cancer
Occult Primary
Ovarian Cancer
Pancreatic Adenocarcinoma
Penile Cancer
Primary Cutaneous Lymphomas
Prostate Cancer
Rectal Cancer
Small Cell Lung Cancer
Soft Tissue Sarcoma
Squamous Cell Skin Cancer
Systemic Light Chain Amyloidosis
NEW Systemic Mastocytosis
T-Cell Lymphomas
Testicular Cancer
Thymomas and Thymic Carcinomas
Thyroid Carcinoma
Uterine Neoplasms
NEW Uveal Melanoma
Vulvar Cancer
Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

NCCN Guidelines For Detection, Prevention, & Risk Reduction

Breast Cancer Risk Reduction
Breast Cancer Screening and Diagnosis
Colorectal Cancer Screening
Genetic/Familial High-Risk Assessment: Breast and Ovarian
Genetic/Familial High-Risk Assessment: Colorectal
Lung Cancer Screening
Prostate Cancer Early Detection

NCCN Guidelines For Supportive Care

Adult Cancer Pain
Antiemesis
Cancer- and Chemotherapy-Induced Anemia
Cancer-Associated Venous Thromboembolic Disease
Cancer-Related Fatigue
Distress Management
NEW Management of Immunotherapy-Related Toxicities
Myeloid Growth Factors
Palliative Care
Prevention and Treatment of Cancer-Related Infections
Smoking Cessation
Survivorship

NCCN Guidelines For Specific Populations

Adolescent and Young Adult (AYA) Oncology
NEW Cancer in People Living with HIV
Older Adult Oncology

NCCN ANNUAL REPORT 2018

Clinical Resources

NCCN Drugs & Biologics Compendium (NCCN Compendium®)

- Contains authoritative, scientifically derived information designed to support decision-making about the appropriate use of drugs and biologics in patients with cancer
- Contains more than 3,200 active records
- Updated in conjunction with the NCCN Guidelines on a continual
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- Subscription-based searchable database online at NCCN.org

NCCN Biomarkers Compendium®

- Contains information designed to support decision-making aroun biomarkers in cancer care
- Provides essential details for tests recommended by the NCCN G as tests that measure changes in genes or gene products for prec monitoring, surveillance, or prognostic information
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NCCN Imaging Appropriate Use Criteria (NCCN Imaging AUC™)

- Details all imaging recommendations included in the NCCN Guide
- Available for more than 50 cancer types in addition to screening a
- NCCN is recognized by Centers for Medicare & Medicaid Services (CMS) as a qualified provider-led entity for creation of the NCCN Imaging AUC™
- Free searchable database online at NCCN.org
- NCCN Imaging AUC™ are available for commercial use through license of the NCCN

>10.1 million downloads in 2018

↑ 26% from 2017

Most Frequently Downloaded NCCN Guidelines in 2018

Breast Cancer	> 790,000 downloads
Non-Small Cell Lung Cancer	> 560,000 downloads
Colon Cancer	> 410,000 downloads

Largest Increase in NCCN Guidelines Downloads in 2018

Ovarian Cancer	60% increase
Neuroendocrine and Adrenal Tumors	60% increase
Esophageal and Esophagogastric Junction Cancers	47% increase

Clinical Resources (continued)

NCCN Radiation Therapy Compendium™

- Includes information designed to support clinical decision-making around the use of radiation therapy in patients with cancer
- Includes a full complement of radiation therapy recommendations found in the current NCCN Guidelines
- Contains 43 disease sites and 848 radiation therapy recommendations
- Subscription-based searchable database online at NCCN.org

NCCN Chemotherapy Order Templates (NCCN Templates®)

- Intended to improve the safe use of drugs and biologics in cancer care
- Includes chemotherapy, immunotherapy, supportive care agents, monitoring parameters, and safety instructions
- Special instructions for self-administered chemotherapeutic agents also provided
- Contains more than 1,330 active templates
- Downloaded ~500,000 times in 2018
- Subscription-based searchable database online at NCCN.org

ANNUAL REPORT TO THE NATION ON STATUS OF CANCER

JNCI JOURNAL of the NATIONAL CANCER INSTITUTE

Annual Report to the Nation on the Status of Cancer, 1999–2015, Featuring Cancer in Men and Women ages 20–49 FREE

Elizabeth Ward, PhD ✉, Recinda L Sherman, PhD, MPH, CTR, S Jane Henley, MSPH, Ahmedin Jemal, DVM, PhD, David A Siegel, MD, MPH, Eric J Feuer, PhD, MS, Albert U Firth, BS, Betsy A Kohler, MPH, CTR, Susan Scott, MPH, Jiemin Ma, PhD, MHS ...
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JNCI: Journal of the National Cancer Institute, djz106,
https://doi.org/10.1093/jnci/djz106
Published: 30 May 2019 **Article history** ▾

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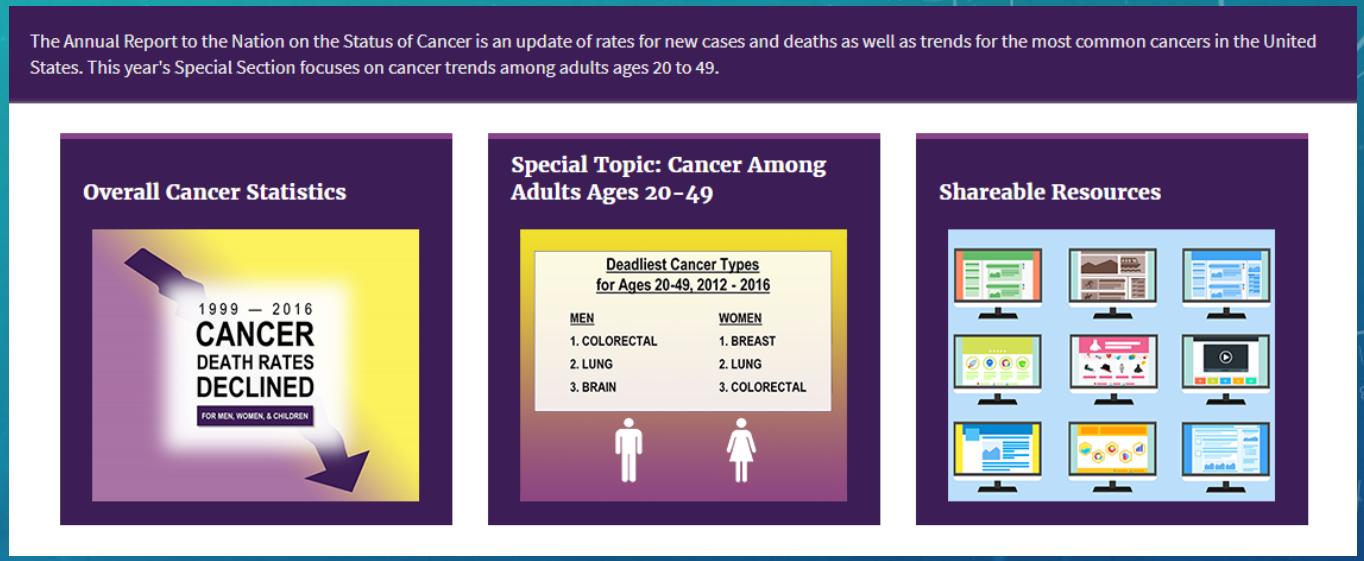
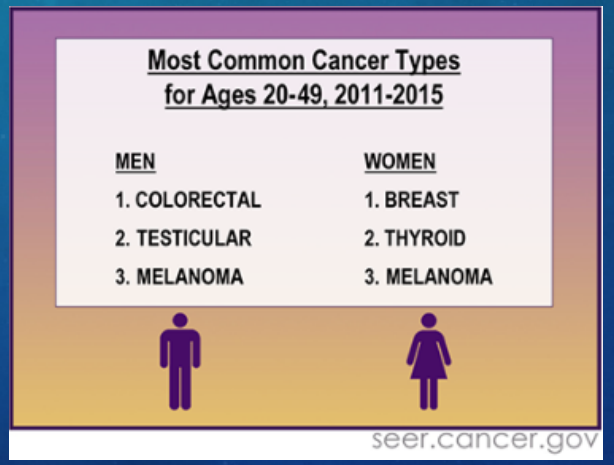
Abstract

Background

The American Cancer Society, Centers for Disease Control and Prevention, National Cancer Institute, and North American Association of Central Cancer Registries (NAACCR) provide annual updates on cancer occurrence and trends by cancer type, sex, race, ethnicity, and age in the US. This year's report highlights the cancer burden among men and women ages 20–49 years.





"Among people of all ages, overall cancer incidence (2011-2015) and death (2012-2016) rates were higher in men than in women, whereas among adults age 20-49 years, incidence and death rates were lower among men than women."

UPDATE ON NATIONAL CANCER MOONSHOT

THE NATIONAL CANCER MOONSHOT INITIATIVE

The National Cancer Moonshot Initiative seeks to accelerate cancer research to make more therapies available to patients while also improving our ability to prevent cancer and detect it at an early stage.

The 21st Century Cures Act, passed in 2016, authorized $1.8 billion over 7 years to fund the Cancer Moonshot. The same year, NCI convened a Blue Ribbon Panel (BRP) of many of the nation's top cancer experts – cancer researchers, oncologists, patient advocates, and private-sector leaders – to give careful thought to what could be done to expedite progress against cancer. To provide recommendations to the National Cancer Advisory Board, the BRP members collaborated with over 100 colleagues from across the cancer research community to identify 10 of the most compelling research opportunities poised for acceleration to help meet the goals of the Cancer Moonshot.

Implementation of the Moonshot is well under way, and over the past two fiscal years Congress has appropriated a total of $600 million for the Cancer Moonshot, which has enabled NCI to support and accelerate research in each of the 10 areas recommended by the BRP. In fiscal year 2017 NCI received its appropriation in May and was able to rapidly invest approximately $277 million in new research opportunities before the end of the fiscal year. NCI issued 17 new Cancer Moonshot funding opportunities in fiscal year 2018 and is in the process of finalizing awards.

The Cancer Moonshot is providing the research community with new resources to pursue critical research questions and to build upon collaborations to ensure their success. These opportunities for acceleration were made possible by decades of investment in basic science and sustained support for the entire cancer research enterprise. Examples of new and ongoing Cancer Moonshot projects include:

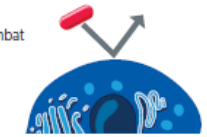
New adult and pediatric translational research immuno-oncology networks

Improving the evidence-based follow-up care for individuals at high risk of cancer due to an inherited genetic susceptibility

Generation of a detailed 3-dimensional map of cancer to inform future cancer research

Creation of a basic and translational research consortium to focus on unique drivers of childhood cancers

Innovative strategies to understand and combat tumor resistance to anticancer therapies



Accelerating colorectal cancer screening and follow-up through multilevel interventions

NCI is currently planning new research opportunities for FY 2019 and beyond. For more information and updates, visit: cancer.gov/moonshot

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NCI MATCH TRIAL MUTATIONS & AGENTS

TABLE 7. Broadening Molecular Profiling Boundaries—Biomarker-Targeted Therapy Matches

TARGETED MUTATION	DRUG
NCI-MATCH trial: NCT02465060[a]	
EGFR activating mutation	Afatinib
HER2 activating mutation	Afatinib
BRCA1 or *BRCA2* mutations	Adavosertib (AZD1775)
FGFR pathway aberrations	AZD4547
NRAS12, *NRAS13*, *NRAS61* mutation	Binimetinib
AKT mutation	Capivasertib (AZD 5363)
PIK3CA mutation	Copanlisib
PTEN mutation	Copanlisib
PTEN loss	Copanlisib
MET amplification	Crizotinib
MET exon 14 deletion	Crizotinib
ALK translocation	Crizotinib
ROS1 translocation or inversion	Crizotinib
BRAF V600E/V600R/V600K/V600D mutation	Dabrafenib + trametinib
DDR2 S768R, I638F, or L239R mutation	Dasatinib
NF2 inactivating mutation	Defactinib
PTEN mutation or deletion and PTEN expression	GSK2636771 (PI3Kβ inhibitor)
PTEN loss	GSK2636771 (PI3Kβ inhibitor)
FGFR mutation or fusion	Erdafitinib
FGFR amplification	Erdafitinib
NTRK1, *NTRK2*, *NRTK3* gene fusions	Larotrectinib (LOXO-101)
Loss of *MLH1* or *MSH2* (by IHC)	Nivolumab
EGFR T790M or rare activating mutation	Osimertinib
CCND1, *CCND2*, *CCND3* amplification & Rb expression	Palbociclib
CDK4 or *CDK6* amplification and Rb protein	Palbociclib
HER2 amplification ≥7 copy numbers	Pertuzumab + trastuzumab
TSC1 or *TSC2* mutation	Sapanisertib
mTOR mutation	Sapanisertib
cKIT exon 9, 11, 13, or 14 mutation	Sunitinib
PIK3CA mutation	Taselisib
GNAQ/*GNA11* mutation	Trametinib
BRAF fusion or *BRAF* non-V600 mutation	Trametinib
NF1 mutation	Trametinib
HER2 amplification	Trastuzumab emtansine
SMO/*PTCH1* mutation	Vismodegib

MOLECULAR TESTING FOR SOLID TUMORS 2019

CA CANCER J CLIN 2019;69:305–343

The Current State of Molecular Testing in the Treatment of Patients With Solid Tumors, 2019

Wafik S. El-Deiry, MD, PhD, FACP[1]; Richard M. Goldberg, MD[2]; Heinz-Josef Lenz, MD, FAPC[3]; Anthony F. Shields, MD, PhD[4]; Geoffrey T. Gibney, MD[5]; Antoinette R. Tan, MD, MHSc[6]; Jubilee Brown, MD[7]; Burton Eisenberg, MD[8,9]; Elisabeth I. Heath, MD, FACP[10]; Surasak Phuphanich, MD[11]; Edward Kim, MD, FACP, FASCO[12]; Andrew J. Brenner, MD, PhD[13]; John L. Marshall, MD [14]

[1]Associate Dean for Oncologic Sciences, Warren Alpert Medical School; Director, Joint Program in Cancer Biology, Brown University and the Lifespan Cancer Institute; Professor of Pathology & Laboratory Medicine and Professor of Medical Science, Brown University, Providence, RI; [2]Professor of Medicine and Director, West Virginia University Cancer Institute, Morgantown, WV; [3]Professor of Medicine, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA; [4]Professor of Oncology, Karmanos Cancer Institute, Detroit, MI; [5]Associate Professor of Medicine, Co-Leader of the Melanoma Disease Group, Lombardi Comprehensive Cancer Institute, MedStar Georgetown Cancer Institute, Washington, DC; [6]Co-Director of Phase I Program, Department of Solid Tumor Oncology and Investigational Therapeutics, Levine Cancer Institute,

Abstract: The world of molecular profiling has undergone revolutionary changes over the last few years as knowledge, technology, and even standard clinical practice have evolved. Broad molecular profiling is now nearly essential for all patients with metastatic solid tumors. New agents have been approved based on molecular testing instead of tumor site of origin. Molecular profiling methodologies have likewise changed such that tests that were performed on patients a few years ago are no longer complete and possibly inaccurate today. As with all rapid change, medical providers can quickly fall behind or struggle to find up-to-date sources to ensure he or she provides optimum care. In this review, the authors provide the current state of the art for molecular profiling/precision medicine, practice standards, and a view into the future ahead. CA Cancer J Clin 2019;69:305-343. © 2019 The Authors. CA A Cancer Journal for Clinicians published by Wiley Periodicals, Inc. on behalf of American Cancer Society. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Keywords: biomarkers, cancer, gene expression profiling, drug target, molecular-targeted therapy, molecular profiling, mutation, precision medicine, sequence analysis

MOLECULAR TESTING FOR SOLID TUMORS 2019

- Includes the Current Recommendations for Biomarker/Molecular Testing for the Following Solid Tumors
- Can be Single Test or Molecular Profiling Assay
  - ANY Solid Tumor – Microsatellite Instability and Mismatch Repair Testing
  - Non-Small Cell Carcinoma of Lung
  - Colon and Rectum
  - Gastric, Esophageal and GE Junction
  - Pancreas
  - Prostate
  - Endometrial
  - Ovarian
  - Breast
  - Brain and Central Nervous System
  - Sarcoma
  - Head and Neck
  - Melanoma
  - Somatic Mutations that could also be Germline Mutations
  - And much more….

TABLE 7. Broadening Molecular Profiling Boundaries—Biomarker-Targeted Therapy Matches

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PIK3CA mutation	Taselisib
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BRAF fusion or *BRAF* non-V600 mutation	Trametinib
NF1 mutation	Trametinib
HER2 amplification	Trastuzumab emtansine
SMO/PTCH1 mutation	Vismodegib

MOLECULAR TESTING FOR SOLID TUMORS 2019

TABLE 1. Predictive Microsatellite Instability/Mismatch Repair Testing for Any Solid Tumor

BIOMARKER	TEST DETECTS	WHEN	TECHNOLOGY	RECOMMENDATIONS	EVIDENCE	CANCER TYPE
MMR	Expression	See *Microsatellite Instability-High Tumors and DNA Mismatch Repair* in the text	IHC	dMMR and MSI-H tests on available tissue are recommended to predict response to pembrolizumab[a]	Lower level; wide acceptance	All
MLH1, *MSH2*, *MSH6*, or *PMS2*	Mutation (= dMMR expression)		NGS	Where applicable, dMMR and MSI-H tests are used together to identify whether a patient should undergo further mutation testing for Lynch syndrome[b]		
MSI	Testing (changes in short repeated DNA sequences)	See *Microsatellite Instability-High Tumors and DNA Mismatch Repair* in the text	PCR, NGS	dMMR and MSI-H tests on available tissue are recommended to predict response to pembrolizumab[a] Where applicable, dMMR and MSI-H tests are used together to identify whether a patient should undergo further mutation testing for Lynch syndrome[b]	Lower level, wide acceptance	All

Abbreviations: dMMR, deficient mismatch repair; IHC, immunohistochemistry; MMR, mismatch repair; MSI, microsatellite instability; MSI-H, microsatellite instability-high; NGS, next-generation sequencing; PCR, polymerase chain reaction.

[a]Nivolumab alone or in combination with ipilimumab may also be an option for patients with colorectal cancer.

[b]dMMR is a characteristic feature of Lynch syndrome, which can play a part in patients (particularly younger patients) with cancers of the gastrointestinal tract (particularly colorectal), endometrium, ovary, brain, breast, and renal pelvis. In Lynch syndrome, dMMR leads to insufficient repair of repetitive DNA sequences and thus a higher risk of multiple malignant tumors.

MOLECULAR TESTING FOR SOLID TUMORS 2019

TABLE 2.1. Currently Recommended Molecular Testing for NSCLC

BIOMARKER	TEST DETECTS	WHEN	TECHNOLOGY	RECOMMENDATIONS	EVIDENCE	CANCER TYPE
ALK	Gene fusion	Metastatic workup	FISH, NGS, RT-PCR[a]	Response to oral ALK TKIs; alectinib has improved efficacy over crizotinib in first line	High-level, wide acceptance	Adenocarcinoma, large cell, NSCLC NOS
	Fusion protein expression		IHC[b]			
		Together with *EGFR* testing in "never smokers" or small/mixed histology specimens		Response to oral ALK TKIs, eg, crizotinib	Lower level, wide acceptance	Squamous cell
EGFR T790M	Mutation	Metastatic workup	NGS, multiple mutation testing	Resistant to EGFR TKIs	High-level, wide acceptance	Adenocarcinoma, large cell, NSCLC NOS
EGFR exon 21 (L858R, L861), exon 20 (S768I), exon 18 (G719X, G719)	Mutation	Metastatic workup	NGS, multiple mutation testing	Sensitive to EGFR TKIs	High-level, wide acceptance	Adenocarcinoma, large cell, NSCLC NOS
					Lower level, wide acceptance	Squamous cell
EGFR exon 19	Deletion	Metastatic workup	NGS, multiple mutation testing	Sensitive to EGFR TKIs	High-level, wide acceptance	Adenocarcinoma, large cell, NSCLC NOS
					Lower level, wide acceptance	Squamous cell
EGFR exon 20 7p12	Insertion mutation	Metastatic workup	NGS, multiple mutation testing	Likely resistant to EGFR TKIs	High-level, wide acceptance	Adenocarcinoma, large cell, NSCLC NOS
					Lower level, wide acceptance	Squamous cell
ROS1	Fusion rearrangement	Metastatic workup	NGS, FISH, RT-PCR	Responsive to ROS1 TKIs	Lower level, wide acceptance	Adenocarcinoma, large cell, squamous cell, NSCLC NOS
PD-L1	Protein expression ≥50%	Metastatic workup	NGS, multiple mutation testing	Response to pembrolizumab in first-line; FDA approved treatment[15]	Lower level, wide acceptance	Adenocarcinoma, large cell, NSCLC, squamous cell NOS
KRAS	Mutation	Metastatic workup	Gene sequencing	Resistance to EGFR TKIs. Gives poor prognosis compared with *KRAS* wt	Lower level, wide acceptance	All NSCLC
BRAF	Mutation, V600E	Metastatic workup	NGS, pyrosequencing, AS-PCR	Emerging targeted agents[19]; responsive to combined BRAF and MEK inhibition	Lower level, wide acceptance	All NSCLC
HER2	Mutation	Anytime	NGS, multiple mutation testing	Emerging targeted agents[20]	Lower level, limited acceptance	All NSCLC
MET	Amplification, mutation	Anytime	NGS, FISH	Emerging targeted agents[21]	Lower level, wide acceptance	All NSCLC
RET	Fusion, rearrangement	Anytime	NGS, FISH, RT-PCR	Emerging targeted agents[22,23]	Lower level, wide acceptance	All NSCLC

Abbreviations: AS-PCR, allele-specific polymerase chain reaction; FDA, US Food and Drug Administration; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NGS, next-generation sequencing; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; PD-L1, programmed death 1 ligand; RT-PCR, reverse transcription-polymerase chain reaction; TKIs, tyrosine kinase inhibitors; wt, wild type.
[a]FISH is the US Food and Drug Administration-approved method for *ALK* gene rearrangement. NGS and RT-PCR currently are not used widely in clinical practice.
[b]IHC can be used as a good alternative to FISH.[24]

MOLECULAR TESTING FOR SOLID TUMORS 2019

TABLE 2.2 Currently Recommended Predictive Molecular Testing for Colon and Rectal Cancers

BIOMARKER	TEST DETECTS	WHEN	TECHNOLOGY	RECOMMENDATIONS	EVIDENCE	CANCER TYPE
KRAS/*NRAS*[a]	Mutation	Workup for metastatic disease (suspected or proven)	NGS[b]	Avoid cetuximab or panitumumab treatment in patients who have tumors with *KRAS* and *NRAS* mutations (exons 2, 3, and 4 in both)	NCCN indicate *lower level, wide acceptance*, but many believe classification is *high-level, wide acceptance*	Metastatic synchronous adenocarcinoma (any T, any N, M1), suspected or documented; *or* Metachronous metastases by CT, MRI, and/or biopsy, documented
BRAF[a]	Mutation V600E	Workup for metastatic disease (suspected or proven)	NGS, pyrosequencing, AS-PCR[b]	Cetuximab or panitumumab treatment is not recommended in patients who have tumors with *BRAF* V600E mutations unless given with a BRAF inhibitor such as vemurafenib The use of irinotecan in combination with cetuximab or panitumumab plus vemurafenib is recommended in all patients with previously treated mCRC	NCCN indicates *lower level, wide acceptance*, but many believe classification is *high-level, wide acceptance*	Metastatic synchronous adenocarcinoma (any T, any N, M1), suspected or documented; *or* Metachronous metastases by CT, MRI, and/or biopsy, documented

Abbreviations: AS-PCR, allele-specific polymerase chain reaction; CT, computed tomography; mCRC, metastatic colorectal cancer; MRI, magnetic resonance imaging; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; PCR, polymerase chain reaction.
[a]*KRAS* and *NRAS* are determined alongside *BRAF* mutations.
[b]Testing can be performed on primary and/or metastatic colorectal tissue specimens.

MOLECULAR TESTING FOR SOLID TUMORS 2019

TABLE 2.7. Currently Recommended Predictive Molecular Testing for Ovarian Cancers[a]

BIOMARKER	TEST DETECTS	WHEN	TECHNOLOGY	RECOMMENDATIONS	EVIDENCE	CANCER TYPE
BRCA1 and *BRCA2*	Mutation	Recurrent disease; initial workup if the patient has a strong family history on initial diagnosis	NGS	Include other homologous recombination pathway genes and MSI or DNA MMR; helps guide therapy (eg, PARP or other DDR enzyme inhibitors; chemotherapy response)	Lower level, wide acceptance	Ovarian cancer
ATM	Mutation	Recurrent disease; initial workup if the patient has a strong family history on initial diagnosis	NGS	Include other homologous recombination pathway genes and MSI or DNA MMR; helps guide therapy (eg, PARP or other DDR enzyme inhibitors; chemotherapy response)	Lower level, wide acceptance	Ovarian cancer
BRIP1	Mutation	Recurrent disease; initial workup if the patient has a strong family history on initial diagnosis	NGS	Include other homologous recombination pathway genes and MSI or DNA MMR; helps guide therapy (eg, PARP or other DDR enzyme inhibitors; chemotherapy response)	Lower level, wide acceptance	Ovarian cancer
CHEK2	Mutation	Recurrent disease; initial workup if the patient has a strong family history on initial diagnosis	NGS	Include other homologous recombination pathway genes and MSI or DNA MMR; helps guide therapy (eg, PARP or other DDR enzyme inhibitors; chemotherapy response)	Lower level, wide acceptance	Ovarian cancer
PALB2	Mutation	Recurrent disease; initial workup if the patient has a strong family history on initial diagnosis	NGS	Include other homologous recombination pathway genes and MSI or DNA MMR; helps guide therapy (eg, PARP or other DDR enzyme inhibitors; chemotherapy response)	Lower level, wide acceptance	Ovarian cancer
RAD51C, *RAD51D*	Mutation	Recurrent disease; initial workup if the patient has a strong family history on initial diagnosis	NGS	Include other homologous recombination pathway genes and MSI or DNA MMR; helps guide therapy (eg, PARP or other DDR enzyme inhibitors; chemotherapy response)	Lower level, wide acceptance	Ovarian cancer

Abbreviations: DDR, DNA damage repair; MMR, mismatch repair; MSI, microsatellite instability; NGS, next-generation sequencing; PARP, poly(adenosine diphosphate-ribose) polymerase.
[a]Approximately 25% of ovarian cancers have germline or somatic mutations in *BRCA*-related or *BRCA*-related genes, including *BRCA1*, *BRCA2*, *PALB2*, *BRIP1*, *RAD51C*, and *RAD51D*. These tumors are targetable by PARP inhibitors, but the US Food and Drug Administration recently extended the approval of the PARP inhibitors niraparib, rucaparib, and olaparib to patients who do not express these mutations.[65-67]

INFORMATION SOURCES AND RESOURCES

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- American Cancer Society; 2019 Cancer Facts and Figures
- AACR Cancer Progress Report 2018; Harnessing Research Discoveries for Patient Benefit
- Update on National Cancer Moonshot Initiative
- NCI Match Trial Mutations and Agents
- 2018 New Drug Approvals Report (/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM629290.pdf)
- ASCO Clinical Cancer Advances 2019 – ASCO's Annual Report on Progress Against Cancer
- Advancing Quality Cancer Care – NCCN 2018 Annual Report
- The Current State of Molecular Testing in the Treatment of Patients With Solid Tumors, 2019; CA CANCER J CLIN 2019;69:305–343
- Cancer Statistics, 2019; CA CANCER J CLIN 2019;69:7–34
- A Blueprint for Cancer Screening and Early Detection: Advancing Screening's Contribution to Cancer Control; CA CANCER J CLIN 2019;69:50–79

QUESTIONS