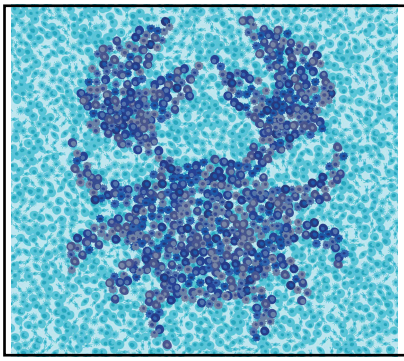
SİTOTOKSİK TEDAVİDEN İMMUNOTERAPİYE

İSTİNYE ÜNİVERSİTESİ

Prof. Dr. Saadettin KILIÇKAP
Tıbbi Onkoloji

liv HOSPITAL ANKARA



Modern çağımızın hastalığı mıdır?

TARİH ÖNCESİ ÇAĞDAN ESKİ MISIRA

From prehistory to ancient Egypt

Cancer has afflicted humanity from pre-historic times though its prevalence has markedly increased in recent decades in unison with rapidly aging populations and, in the last half-century, the increasing risky health behavior in the general population and the increased presence of carcinogens in the environment and in consumer products. The oldest credible evidence of cancer in mammals consists of tumor masses found in fossilized dinosaurs and human bones from pre-historic times. Perhaps the most compelling evidence of cancer in dinosaurs emanates from a recent large-scale study that screened by fluoroscopy over 10,000 specimens of dinosaur vertebrae for evidence of tumors and further assessed abnormalities by computerized tomography (CT).[1] Out of several species of dinosaurs surveyed, only *cretaceous hadrosaurs* (duck-billed dinosaurs), that lived ~70 million years ago, harbored benign tumors (hemangiomas" desmoplastic fibromas[2] and osteoblastomas[3] but 0.2% of specimens exhibited malignant metastatic disease.

Key words: cancer, history, pioneers, landmarks, milestones
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[1]benign vascular tumors;
[2]benign fibrous tumors of bone.

The earliest written record generally regarded as describing human cancer appeared in ancient Egyptian manuscripts discovered in the 19th century, especially the Edwin Smith and George Ebers papyri that describe surgical, pharmacological, and magical treatments. They were written between 1500 and 1600 BC possibly based on material from thousands of years earlier. The Smith papyrus, possibly written by Imhotep the physician-architect who designed and built the step pyramid at Sakkara in the 30th century BC under Pharaoh Djoser, is believed to contain the first reference to breast cancer (case 45) when referring to tumors of the anterior chest. It warns that when such tumors are cool to touch, bulging, and have spread over the breast no treatment can succeed.[7] It also provides the earliest mention of wound suturing and of using a "fire drill" to cauterize open wounds. In ancient times, gods were thought to preside over human destiny, including health and disease, medicine and religion were intertwined, practiced by priests and sages who often were revered as gods' intermediaries. For instance, in case 1 of the Edwin Smith papyrus caregivers are called "lay-priests of Sekhmet;" the feared lion-headed "lady of terror" and one of the oldest Egyptian deities also known as the "lady of life" patron of caregivers and healers.[7]

The earliest cancerous growths in humans were found in Egyptian and Peruvian mummies dating back to ~1500 BC. The oldest scientifically documented case of disseminated cancer was that of a 40- to 50-year-old Scythian king who lived in the steppes of Southern Siberia ~2,700 years ago.

Desmoplastic fibrom Osteoblastoma

30 th century BC Breast cancer

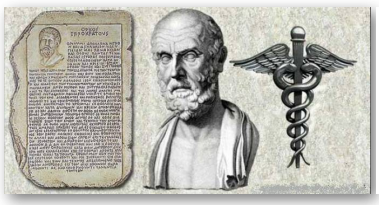
2700 years ago King of Siberian

ESKİ MISIRDA MUMYALAR

the cancerous nature of his disseminated skeletal lesions and their prostatic origin.[4] Half a millennium later and half a world away, a Ptolemaic Egyptian was dying of cancer.[5] Digital radiography and multi-detector CT scans of his mummy, kept at the Museu Nacional de Arqueologia in Lisbon, determined that his cancer was disseminated. The morphology and distribution of his lesions (spine, pelvis, and proximal extremities), and the mummy's gender and age suggest prostate as the most likely origin.

Prostat kanseri

HIPPOCRATES



From ancient Egypt to Greece and Rome

Following the decline of Egypt and Greece, Roman medicine became preeminent, especially with Hippocrates of Kos (460-c.360BC), an island off the coast of Turkey, and Claudius Galenus (AD129–c.216), better known as Galen of Pergamum (modern-day Bergama, Turkey). Writings attributed to them, describing life-long experiences and observations, became the foundation and repository of medical knowledge for the ensuing 1,500 years.

Hippocrates. Little is known with certainty about who he was, how he practiced medicine, and which writings attributed to him are his. The little we know about Hippocrates we owe to his first biographer Soranus of Ephesus (a 2nd century AD Greek physician) and to Aristotle (384–322BC) who refers to him as *The Great Hippocrates*. His current image emerged in the sixteenth Century after "…[being] constantly invented and reinvented; constructed, decon-

KANSERİN HİKAYESİ

Aulus Cornelius Celsus (25BC-AD50), was a Roman physician and prominent Hippocrates successor. He described the evolution of tumors from surgically resectable *cacethes* followed by unresponsive *carcinos* (he later called *carcinomas*) and fungated ulcers he advocated should be left alone[15] because "the excised carcinomas have returned and caused death."[15] He explained, "It is only the cacoethes which can be removed; the other stages are irritated by treatment; and the more so the more vigorous it is. Some have used caustic medicaments, some the cautery, some excision with a scalpel; but no medicament has ever given relief; the parts cauterized are excited immediately and increase until they cause death."

Celsus acknowledged that only rare could differentiate cacoethes from carcinomas, "No one, however, except by time and experiment, can have the skill to distinguish a cacoethes which admits of being treated from a carcinoma which does not." He vividly described the invasive nature of carcinomas, "This also is a spreading disease. And all these signs often extend, and there results from them an ulcer which the Greeks call phagedaena because it spreads rapidly and penetrates down to the bones and so devours the flesh." Reportedly, he is the first to attempt reconstructive surgery following excision of cancer.

the city in 166, the year the plague (possibly smallpox) struck. Two years later, Roman Emperor Marcus Aurelius summoned him to serve as army surgeon during an outbreak among troops stationed at Aquileia (168–169) and when the plague extended to Rome, he was appointed personal physician to the Emperor and his son Commodus adding luster and fame to his fast rising career.

While medical practitioners of the time disagreed on whether experience or established theories should guide treatment, he applied Aristotelian empiricism by ensuring that established theories gave meaning to personal observations and relied on logic to sort out uncertainties and discover medical truths. Galen was the first to recognize the difference between arterial (bright) and venous (dark) blood he postulated to be distinct systems originating from the heart and the liver, respectively. He used vivisections to study body functions. For instance, when he cut the laryngeal nerve of a pig the animal stopped squealing; a nerve now known as *Galen's Nerve*. Likewise, by tying the ureters he showed that urine came from kidneys and that severing spinal cord nerves caused paralysis. He performed audacious and delicate operations, such as removal of the lens to treat cataracts, an operation that would become commonplace 2,000 years later. His pioneering anatomical studies, based on dissecting pigs and

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- Cerrahi
- Hormonal tedavi (1896)
- Radyasyon tedavisi (1911)
- Kemoterapi (1945)
- Adjuvant tedavi
- Antiangiogenesis tedavi
- Targeted terapiler
- Immunoterapi
- Nanoteknoloji
- Genomics, proteomics,
- … mics
- …….

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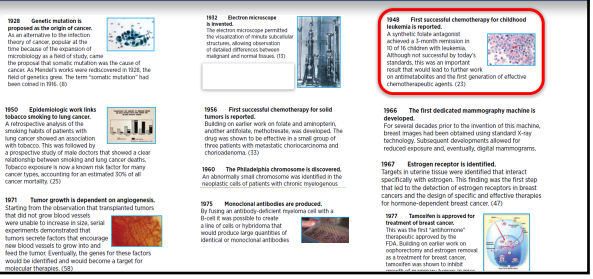

1928 Genetic mutation is proposed as the origin of cancer.
As an alternative to the infection theory of cancer, popular at the time because of the expansion of microbiology as a field of study, came the proposal that somatic mutation was the cause of cancer. As Mendel's works were rediscovered in 1928, the field of genetics grew. The term "somatic mutation" had been coined in 1910. (8)

1932 Electron microscope is invented.
The electron microscope permitted the visualization of minute subcellular structures, allowing observation of detailed differences between malignant and normal tissues. (15)

1948 First successful chemotherapy for childhood leukemia is reported.
A synthetic folate antagonist achieved a 3-month remission in 10 of 16 children with leukemia. Although not successful by today's standards, this was an important result that would lead to further work on antimetabolites and the first generation of effective chemotherapeutic agents. (25)

1950 Epidemiologic work links tobacco smoking to lung cancer.
A retrospective analysis of the smoking habits of patients with lung cancer showed an association with tobacco. This was followed by a prospective study of male doctors that showed a clear relationship between smoking and lung cancer deaths. Tobacco exposure is now a known risk factor for many cancer types, accounting for an estimated 30% of all cancer mortality. (25)

1956 First successful chemotherapy for solid tumors is reported.
Building on earlier work on folate and aminopterin, another antifolate, methotrexate, was developed. The drug was shown to be effective in a small group of three patients with metastatic choriocarcinoma and choroadenoma. (33)

1960 The Philadelphia chromosome is discovered.
An abnormally small chromosome was identified in the neoplastic cells of patients with chronic myelogenous

1966 The first dedicated mammography machine is developed.
For several decades prior to the invention of this machine, breast images had been obtained using standard X-ray technology. Subsequent developments allowed for reduced exposure and, eventually, digital mammograms.

1967 Estrogen receptor is identified.
Targets in uterine tissue were identified that interact specifically with estrogen. This finding was the first step that led to the detection of estrogen receptors in breast cancers and the design of specific and effective therapies for hormone-dependent breast cancer. (47)

1971 Tumor growth is dependent on angiogenesis.
Starting from the observation that transplanted tumors that did not grow blood vessels were unable to increase in size, serial experiments demonstrated that tumors secrete factors that encourage new blood vessels to grow into and feed the tumor. Eventually, the genes for these factors would be identified and would become a target for molecular therapies. (58)

1975 Monoclonal antibodies are produced.
By fusing an antibody-deficient myeloma cell with a B-cell it was possible to create a line of cells or hybridoma that would produce large quantities of identical or monoclonal antibodies

1977 Tamoxifen is approved for treatment of breast cancer.
This was the first "antihormone" therapeutic approved by the FDA. Building on earlier work on oophorectomy and estrogen removal as a treatment for breast cancer, tamoxifen was shown to inhibit

KANSERDE SON 100 YIL

2012 Major checkpoint inhibitor shows dramatic clinical trial results.
An anti–PD-1 monoclonal antibody drastically shrank tumors in patients with melanoma, kidney cancer, and advanced non-small cell lung cancer. (167)

2015 The Precision Medicine initiative is announced.
The Precision Medicine Initiative leverages advances in genomics, methods for managing and analyzing large data sets, and health information technology to accelerate biomedical discoveries and bring precision medicine to many aspects of health care, including cancer.

2015 Vice President Joe Biden announces that he will forgo a run for the U.S. presidency to dedicate his energy to "a moonshot in this country to cure cancer…an absolute national commitment to end cancer as we know it today."
In a statement, AACR CEO Margaret Foti, PhD, MD (hc) notes that "the vice president is absolutely correct: We are at a turning point in cancer research, … [but] future progress for cancer patients will require more research and more funding for the federal agencies that are vital for fueling progress against cancer, in particular, the NIH, NCI, and FDA."

2012 Breakthrough Therapy designation is established for the FDA.
This designation expedites the development and review of drugs that treat a serious or life-threatening disease or condition and provide substantial improvement over existing therapies.

2015 Mutation signatures of in vitro carcinogen exposure are extracted from mammalian genome.
Mutational processes leave characteristic marks on the genome, creating a record of the mutagenic processes that occur throughout the life of an organism. Earlier

2016 The FDA approves the first liquid biopsy test.
The FDA approved a liquid biopsy test, a companion diagnostic test called cobas EGFR Mutation Test v2. The test uses plasma samples to identify patients with metastatic non-small cell lung cancer (NSCLC) eligible for treatment with the EGFR-targeted therapeutic erlotinib (Tarceva). The need for this noninvasive test is particularly important in cases in which a tumor biopsy is not possible. (185)

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MEDİKAL ONKOLOG NE İSTER?

Daha uzun süreli sağkalım - KÜR

Daha iyi yaşam kalitesi

Minimum invaziv girişimle en geniş moleküler tümör paneli

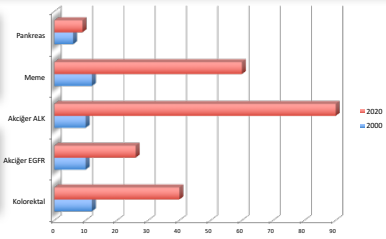
Hızlı raporlama süreci

En iyi ilaca en kısa sürede ulaşma

DEĞİŞİM KLİNİĞE NASIL YANSIDI?

HER HASTAYA AYNI TEDAVİ

HEDEFLİ TEDAVİLER İMMUNOTERAPİLER



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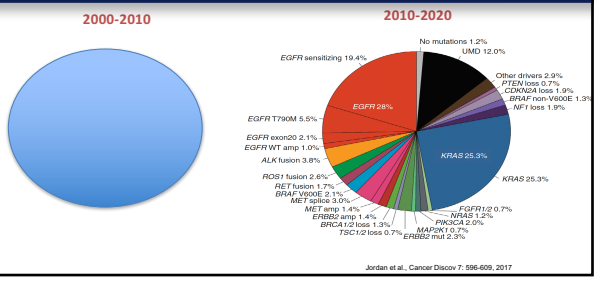
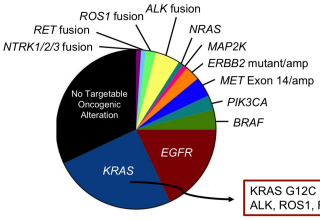
MUTASYON (EGFR, BRAF, ...)	cfDNA
FÜZYON (NTRK)	CTC
MSI	BRCA
PDL1	DİRENÇ MUTASYONLARI (P53)
TMB	IMMUN-SKOR

AKCİĞER KANSERİNDE HİSTOLOJİ VE DÜRÜCÜ MUTASYONLAR



Jordan et al., Cancer Discov 7: 596-609, 2017

Precision Therapy for Lung Adenocarcinoma in 2021



Target	Approved Drug(s)
EGFR	Gefitinib, Erlotinib, Afatinib, Dacomitinib, Osimertinib, Erlotinib/Ramucirumab
ALK	Crizotinib, Ceritinib, Alectinib, Brigatinib, Lorlatinib
ROS1	Crizotinib, Entrectinib
NTRK 1/2/3	Latrotrectinib, Entrectinib
RET	Selpercatinib, Pralsetinib
MET exon 14	Capmatinib
BRAF V600E	Dabrafenib/Trametinib

KRAS G12C ~ 50% of KRAS mutations. More patients than ALK, ROS1, RET and TRK 1/2/3 combined !

KRAS is the largest subset of NSCLC with an oncogenic alteration without an approved targeted therapy

TARGETED TERAPİLER

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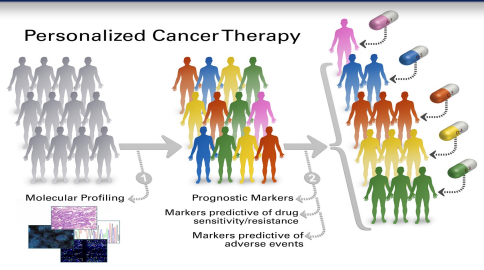

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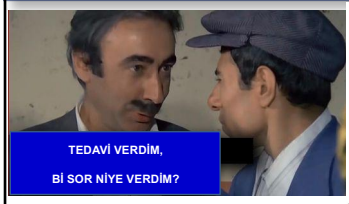
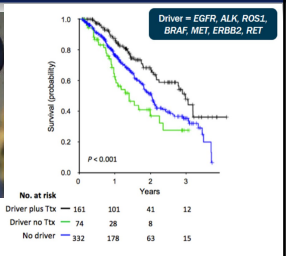
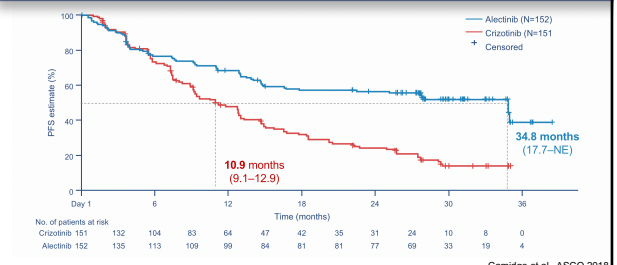




Aisner DL, et al. *Clin Cancer Res.* 2018;24:1038-1047.

ALK POZİTİF HASTADA EN UZUN SÜRELİ PFS



Camidge et al., ASCO 2018

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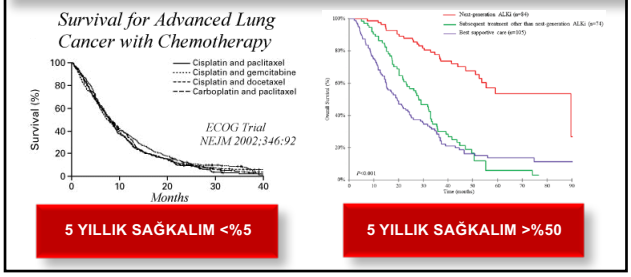
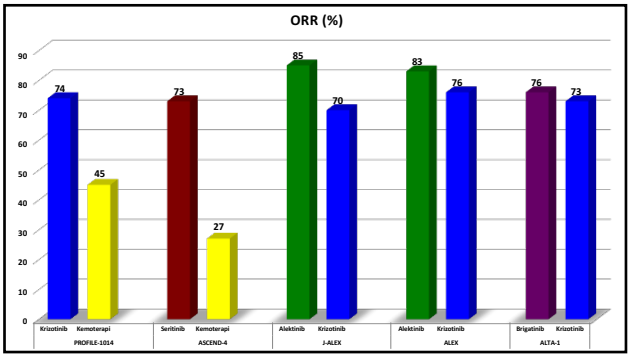
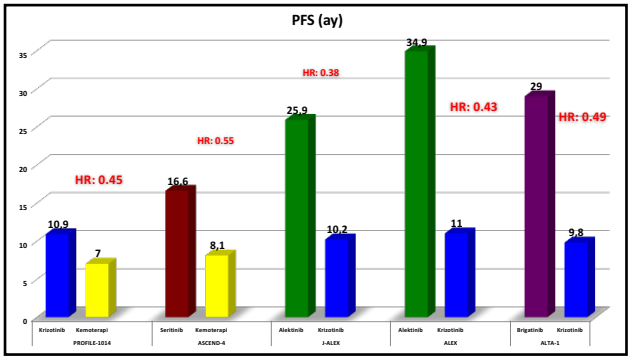


5 YILLIK SAĞKALIM <%5

5 YILLIK SAĞKALIM >%50





Lorlatinib – a potent ALK TKI covering the broadest range of ALK resistance mutations

- Secondary mutations in the ALK domain can induce resistance to first- and second-generation ALK TKIs[1]
- Lorlatinib is a selective inhibitor of ALK and ROS1 with broad-spectrum potency against most known ALK resistance mutations, including G1202R[1,2]

Cellular ALK Phosphorylation Mean IC_{50} (nM)

Mutation Status	Crizotinib	Ceritinib	Alectinib	Brigatinib	Lorlatinib
Parental BA/F3	763.9	885.7	890.1	2774.0	11293.8
V1	38.6	4.9	11.4	10.7	2.3
C1156Y	61.9	5.3	11.6	4.5	4.6
I1171N	130.1	8.2	397.7	26.1	49.0
I1171S	94.1	3.8	177.0	17.8	30.4
I1171T	51.4	1.7	33.6	6.1	11.5
F1174C	115.0	38.0	27.0	18.0	8.0
L1196M	339.0	9.3	117.6	26.5	34.0
L1198F	0.4	196.2	42.3	13.9	14.8
G1202R	381.6	124.4	706.6	129.5	49.9
G1202del	58.4	50.1	58.8	95.8	5.2
D1203N	116.3	35.3	27.9	34.6	11.1
E1210K	42.8	5.8	31.6	24.0	1.7
G1269A	117.0	0.4	25.0	ND	10.0

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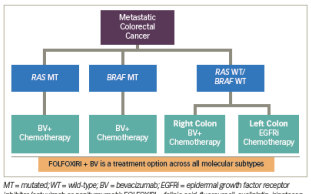
Figure 1: First-line treatment algorithm in good performance patients with metastatic colorectal cancer

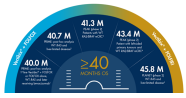


MT = mutated; WT = wild-type; BV = bevacizumab; EGFR = epidermal growth factor receptor inhibitor (cetuximab or panitumumab); FOLFOXIRI = folinic acid, fluorouracil, oxaliplatin, irinotecan.

Vectibix® has demonstrated a median overall survival of more than 40 months in several subgroups* from 5 analyses with FOLFOX and FOLFIRI, including patients with left-sided primary tumours.[1-5]

WITH VECTIBIX®: MEDIAN OVERALL SURVIVAL ≥40 MONTHS[1-5]

with FOLFOX or FOLFIRI in different patient subgroups such as:



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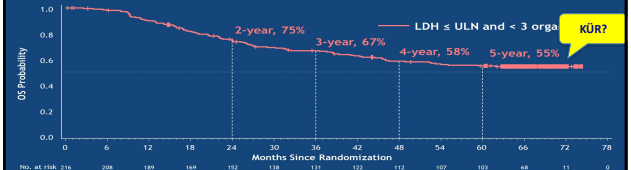
Dabrafenib Plus Trametinib: OS in Patients With Normal LDH and < 3 Organ Sites



Presented By Paul Nathan at 2019 ASCO Annual Meeting

Previously Treated Advanced HER2-Positive BC

Recent FDA Approvals

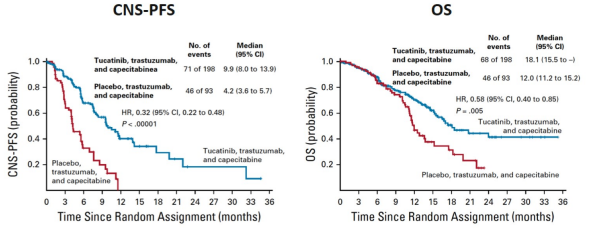
Date	Drug	Type	Indication
Dec 20, 2019	Trastuzumab deruxtecan	HER2-directed antibody and topoisomerase inhibitor	Treatment of patients with unresectable or metastatic HER2-positive BC who have received 2 or more anti-HER2-based regimens in the metastatic setting[a]
Feb 25, 2020	Neratinib	Kinase inhibitor	In combination with capecitabine for treatment of patients with advanced or metastatic HER2-positive BC who have received 2 or more anti-HER2-based regimens in the metastatic setting[b]
Apr 17, 2020	Tucatinib	Kinase inhibitor	In combination with trastuzumab and capecitabine for treatment of patients with advanced unresectable or metastatic HER2-positive BC, including patients with brain mets, who have received 1 or more anti-HER2-based regimens in metastatic setting[c]
Dec 16, 2020*	Margetuximab	HER2/neu receptor antagonist	In combination with chemotherapy for treatment of patients with metastatic HER2-positive BC who have received 2 or more anti-HER2 regimens, at least 1 of which was for metastatic disease[d]

New Challenge: What is the optimal sequencing of these therapies to give patients the maximum benefit?

*Approved after recording of this activity.
a. Enhertu® (fam-trastuzumab deruxtecan-nxki) [PI]. Daiichi Sankyo; 2019; b. Nerlynx® (neratinib) [PI]. Puma Biotechnology, Inc; 2020; c. Tukysa™ (tucatinib) [PI]. Seattle Genetics, Inc; 2020; d. Margenza™ (margetuximab-cmkb) [PI]. MacroGenics, Inc; 2020.

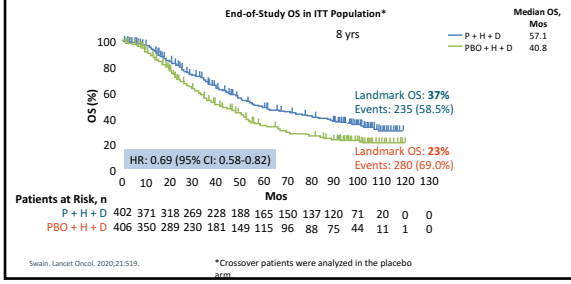
HER2CLIMB

Intracranial Efficacy and Survival in Patients With Brain Mets



Lin NU, et al. *J Clin Oncol*. 2020;38:2610-2619.

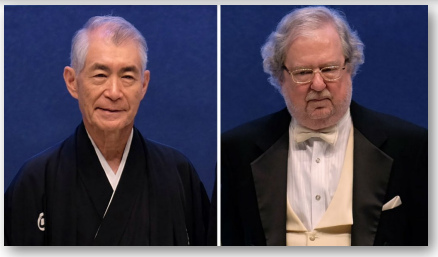
CLEOPATRA: Standard First-line Treatment for HER2+ MBC With Pertuzumab, Trastuzumab, and Docetaxel



Swain. Lancet Oncol. 2020;21:519.

*Crossover patients were analyzed in the placebo arm.

NOBEL PRIZE- IMMUN-CHECKPOINT



EMPOWER-Lung 1: Clinical benefits of first-line (1L) cemiplimab monotherapy by PD-L1 expression levels in patients with advanced NSCLC

Saadettin Kilickap,[1] Ahmet Sezer,[2] Mahmut Gümüş,[3] Igor Bondarenko,[4] Mustafa Özgüroğlu,[5] Miranda Gogishvili,[6] Haci M Turk,[7] Irfan Cicin,[8] Dmitry Bentsion,[9] Oleg Gladkov,[10] Philip Clingan,[11] Virote Sriuranpong,[12] Naiyer Rizvi,[13] Siyu Li,[14] Sue Lee,[14] Tamta Makharadze,[15] Semra Paydas,[16] Marina Nechaeva,[17] Frank Seebach,[18] David M Weinreich,[18] George D Yancopoulos,[18] Giuseppe Gullo,[18] Israel Lowy,[18] Petra Rietschel[18]

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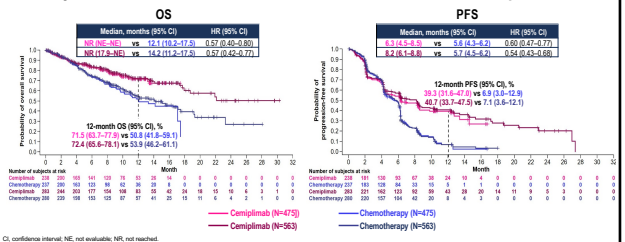
Primary Outcomes Were Similar Between the N=475 and N=563 Populations



CI, confidence interval; NE, not evaluable; NR, not reached.

2021 ASCO ANNUAL MEETING

Nivolumab plus ipilimumab or nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced esophageal squamous cell carcinoma: first results of the CheckMate 648 study

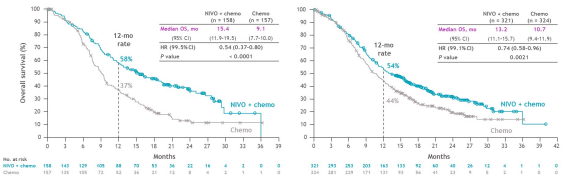
Ian Chau,[1] Yuichiro Doki,[2] Jaffer A. Ajani,[3] Jianming Xu,[4] Lucjan Wyrwicz,[5] Satoru Motoyama,[6] Takashi Ogata,[7] Hisato Kawakami,[8] Chih-Hung Hsu,[9] Antoine Adenis,[10] Farid el Hajbi,[11] Maria Di Bartolomeo,[12] Maria Ignez Braghiroli,[13] Eva Holtved,[14] Ioannis Xynos,[15] Xuan Liu,[15] Ming Lei,[15] Kaoru Kondo,[15] Ken Kato,[16] Yuko Kitagawa[17]

[1]Royal Marsden Hospital, London & Surrey, UK; [2]Osaka University Graduate School of Medicine, Osaka, Japan; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Affiliated Hospital Cancer Center, Academy of Military Medical Sciences, Beijing, China; [5]Klinika Onkologii i Radioterapii, Narodowy Instytut Onkologii, Warszawa, Poland; [6]Akita University Hospital, Akita, Japan; [7]Kanagawa Cancer Center, Kanagawa, Japan; [8]Kindai University Faculty of Medicine, Osakasayama, Japan; [9]National Taiwan University Hospital, Taipei, Taiwan; [10]Institut du Cancer de Montpellier, Montpellier, France; [11]Centre Oscar Lambret, Lille, France; [12]Fondazione IRCCS Instituto Nazionale dei Tumori, Milan, Italy; [13]Institute of Cancer of São Paulo, University of São Paulo, São Paulo, Brazil; [14]Odense University Hospital, Odense, Denmark; [15]Bristol Myers Squibb, Princeton, NJ; [16]National Cancer Center Hospital, Tokyo, Japan; [17]Keio University School of Medicine, Tokyo, Japan

Abstract Number LBA4001

CheckMate 648

Overall survival: NIVO + chemo vs chemo



- Superior OS with NIVO + chemo vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 46% reduction in the risk of death and a 6.3-month improvement in median OS
  - All randomized: 26% reduction in the risk of death and a 2.5-month improvement in median OS

[a]Minimum follow-up 12.9 months.

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Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study

	Nivo-Kemo		Kemo		Nivo-Ipi
OS	13.4	HR 0.54	9.1	HR 0.64	13.7
PFS	6.9	HR 0.65	4.4	HR 1.02	4.0
DoR	8.4		5.7		11.8
ORR	%53		%20		%35

2021 ASCO ANNUAL MEETING

Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

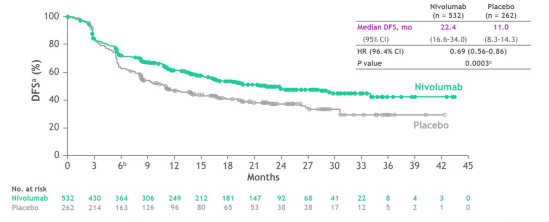
Ronan J. Kelly,[1] Jaffer A. Ajani,[2] Jaroslaw Kuzdzal,[3] Thomas Zander,[4] Eric Van Cutsem,[5] Guillaume Piessen,[6] Guillermo Mendez,[7] Josephine Feliciano,[8] Satoru Motoyama,[9] Astrid Lièvre,[10] Hope Uronis,[11] Elena Elimova,[12] Cecile Grootscholten,[13] Karen Geboes,[14] Jenny Zhang,[15] Samira Soleymani,[15] Ming Lei,[15] Prianka Singh,[15] James M. Cleary,[16] Markus Moehler[17]

[1]The Charles A. Sammons Cancer Center at Baylor University Medical Center, Dallas, TX; [2]The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Jagiellonian University, John Paul II Hospital, Cracow, Poland; [4]University Hospital of Cologne, Cologne, Germany; [5]University Hospitals Gasthuisberg, Leuven and KULeuven, Leuven, Belgium; [6]University of Lille, Claude Huriez University Hospital, Lille, France; [7]Fundacion Favaloro, Buenos Aires, Argentina; [8]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; [9]Akita University Hospital, Akita, Japan; [10]CHU Pontchaillou, Rennes 1 University, Rennes, France; [11]Duke Cancer Institute, Durham, NC; [12]Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [14]UZ Gent, Gent, Belgium; [15]Bristol Myers Squibb, Princeton, NJ; [16]Dana Farber Cancer Institute, Boston, MA; [17]Johannes-Gutenberg University Clinic, Mainz, Germany

Abstract number 4003

CheckMate 577

Disease-free survival (DFS)



- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

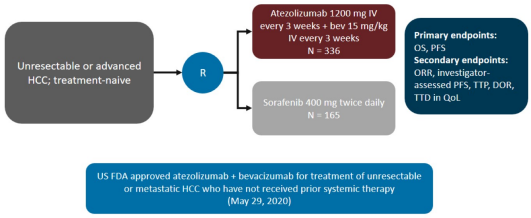
[a]Per investigator assessment; [b]6-month DFS rates were 72% (95% CI, 68-76) in the nivolumab arm and 63% (95% CI, 57-69) in the placebo arm; [c]The boundary for statistical significance at the prespecified interim analysis required the *P* value to be less than 0.036.
Kelly RJ, et al. *N Engl J Med* 2021;384:1191-1203.

5

Adjuvant nivolumab (NIVO) in resected esophageal or gastroesophageal junction cancer (EC/GEJC) following neoadjuvant chemoradiotherapy (CRT): Expanded efficacy and safety analyses from CheckMate 577.

	Nivo		Plasebo
DFS	22.4	HR 0.69	11.0
DMFS	28.3	HR 0.74	17.6
PFS2	NR	HR 0.77	32.1

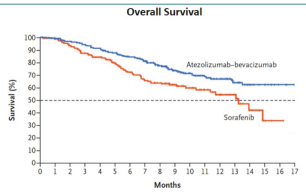
IMbrave150: Atezolizumab-Bevacizumab in Advanced HCC
Phase 3 Study Design



US FDA approved atezolizumab + bevacizumab for treatment of unresectable or metastatic HCC who have not received prior systemic therapy (May 29, 2020)

Cheng A-L, et al. *Ann Oncol*. 2019;30:ix186-ix187.

IMbrave150: Atezolizumab-Bevacizumab in Advanced HCC
Overall Survival

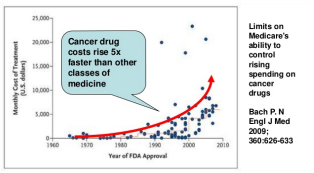


Median Overall Survival (95% CI)
Atezolizumab-Bevacizumab: NE
Sorafenib: 13.2 (10.4, NE)
HR 0.58 (95% CI: 0.42, 0.79); *P* < .001

Median duration of follow-up, 8.6 months.
Finn RS, et al. *N Engl J Med*. 2020;382:1894-1905.

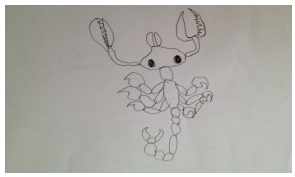
Uzamış Sağkalım – Daha Fazla Maliyet

Cost of cancer drugs by year of approval



Limits on Medicare's ability to control rising spending on cancer drugs

Bach P. N Engl J Med 2009; 360:626-633



TEŞEKKÜRLER...