Great Debates
Solid Tumors

2025

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Miami

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Solid Tumors

Target over Tissue: The Rise of Tumor-Agnostic Cancer Therapies

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Disclosures

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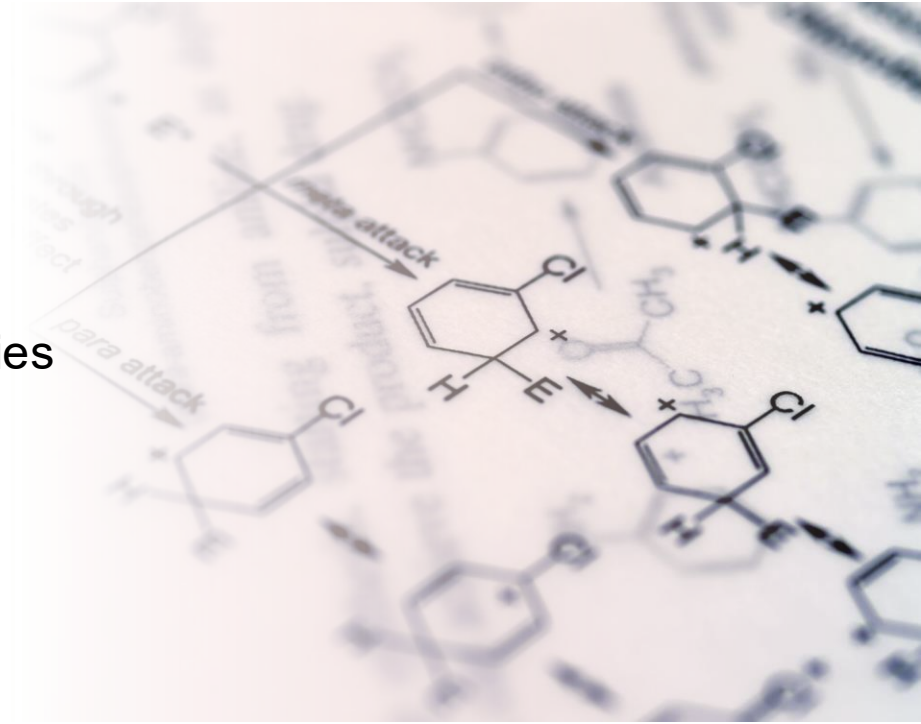
Learning Objectives

- Summarize the rationale, biomarkers, and clinical promise of tumor-agnostic therapies in advancing precision oncology across diverse cancer types
- Assess the efficacy, safety profiles, mechanisms of action, and clinical indications of newer and emerging tumor-agnostic agents
- Describe key challenges in tumor-agnostic care and strategies for addressing barriers to broader clinical adoption

Agenda

- Emergence of tumor-agnostic therapy
- 3 examples
- 3 emerging new tumor-agnostic therapies
- Challenges



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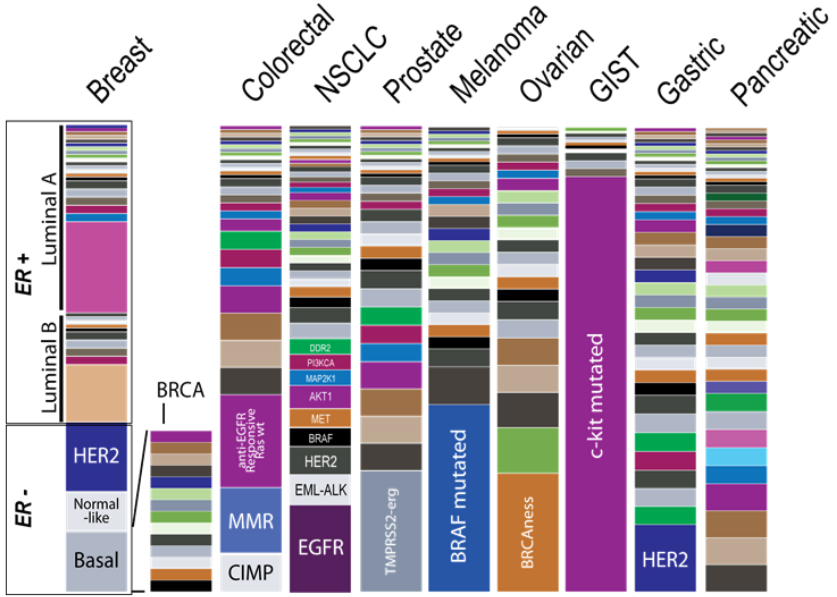
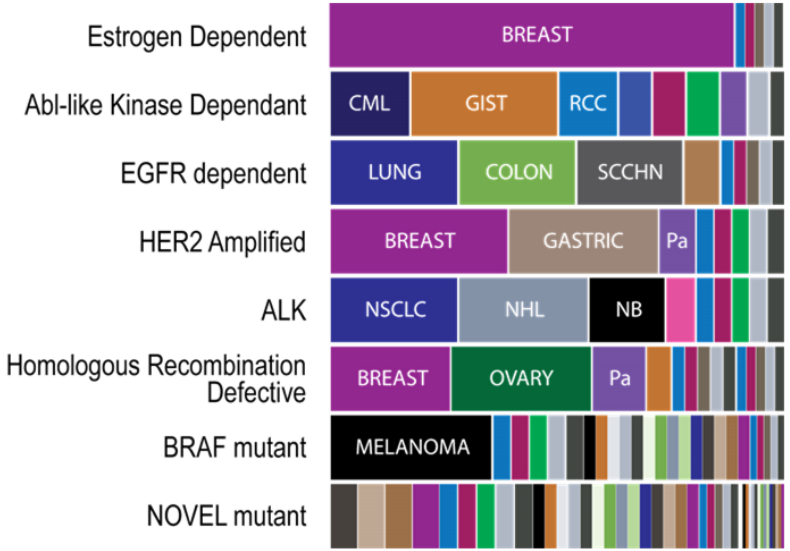
How It All Began...

- Historically, cancer has been defined by its site of origin
- Today, certain cancers are increasingly being defined by genomic alterations (eg, point mutations, gene fusions) capable of driving proliferation



- Precision oncology defines cancers by their common genetic changes



NSCLC = non-small cell lung cancer; GIST = gastrointestinal stromal tumor; CML = chronic myeloid leukemia; RCC = renal cell carcinoma; SCCHN = squamous cell carcinoma of the head and neck; Pa = pancreatic cancer; NHL = ; non-Hodgkin lymphoma; NB = neuroblastoma.

Slide courtesy Rodon J. Biankin AV, et al. *Nature*. 2015;526(7573):361-370.

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How It All Began...

WHAT WAS APPROVED

- 2017: **pembrolizumab** for patients with tumors deficient in mismatch repair (**MMR**) or with high microsatellite instability (MSI)
- 2018: **larotrectinib** for patients with ne receptor tyrosine kinase (**NTRK**) fusio tumors
- 2019: entrectinib in patients with NTI tumors
- 2020: pembrolizumab for patients a with high tumor mutational burden
- 2021: dostarlimab-gxly for patient repair deficient tumors
- **2022: FDA draft for industry**
- 2022: **dabrafenib + trametinib** in patients wi **V600E** mutated tumors
- 2022: **selpercatinib** in patients with rearranged during transfection (**RET**) fusion-positive tumors


Tissue Agnostic Drug Development in Oncology
Guidance for Industry
DRAFT GUIDANCE
This guidance document is being distributed for comment purposes only.
U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
October 2022
Clinical/Medical

WHAT WAS NOT APPROVED

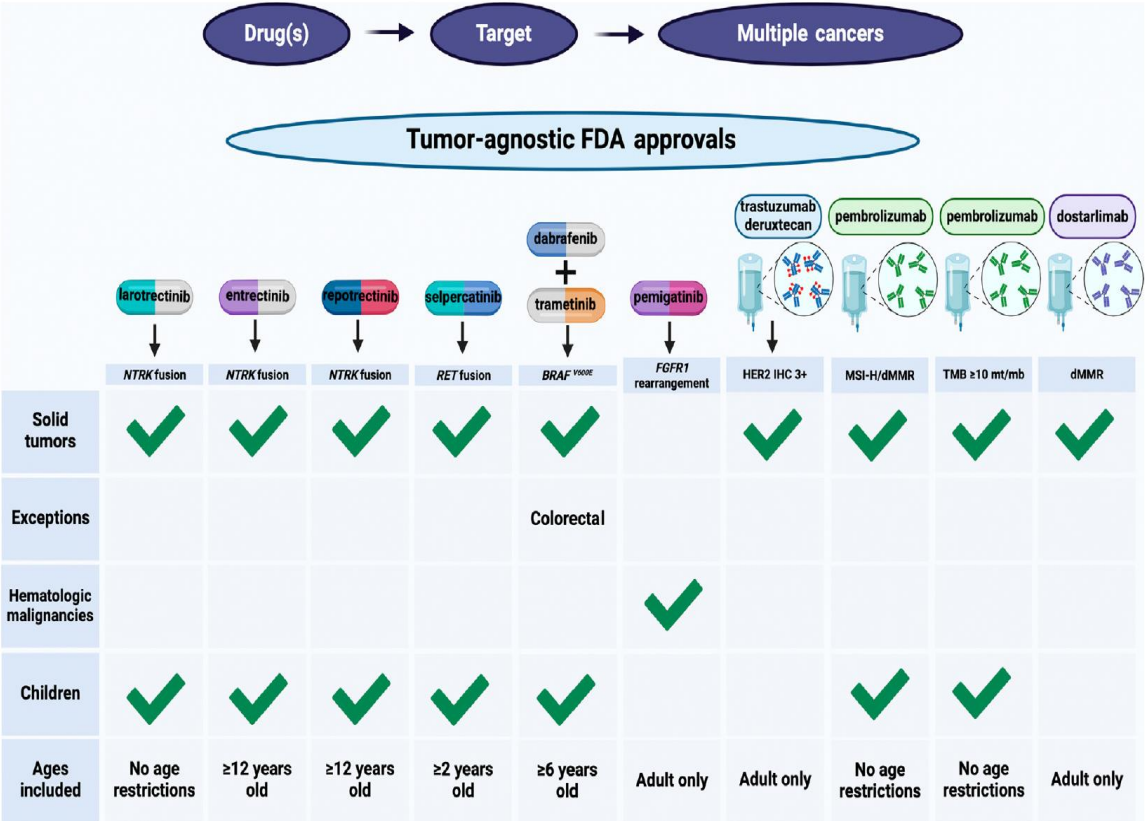
- BRAF monotherapy (CRC as an exception)
- HER2 mut and neratinib
- FGFR
- PI3K inhibitors
  - And many more…

WORK IN PROGRESS…

- *NRG1 fusions and HER2-3 inhibitors?*
- *ALK and ALK inhibitors?*
- *ROS1 and ROS1 inhibitors?*
- *TSC1/2 mut and Nab-Sirolimus?*
- *FGFR inhibitors*
  - *In FGFR2 fusions?*
  - *In FGFR alt?*
- *HER2*
  - *HER2 ampl?*
  - *HER2 mut?*
  - *EGFR/HER2 exon 20 muts?*
  - *HER2 low and low and trastuzumab deruxtecan?*
- ***panRAS??***

FDA = US Food and Drug Administration; CRC = colorectal cancer.
Slide courtesy Rodon J.

There Are 9 Drugs Approved in 6 Tumor-Agnostic Indications



Kudek MR, et al. *Trends Cancer*. 2025;11(8):726-735.

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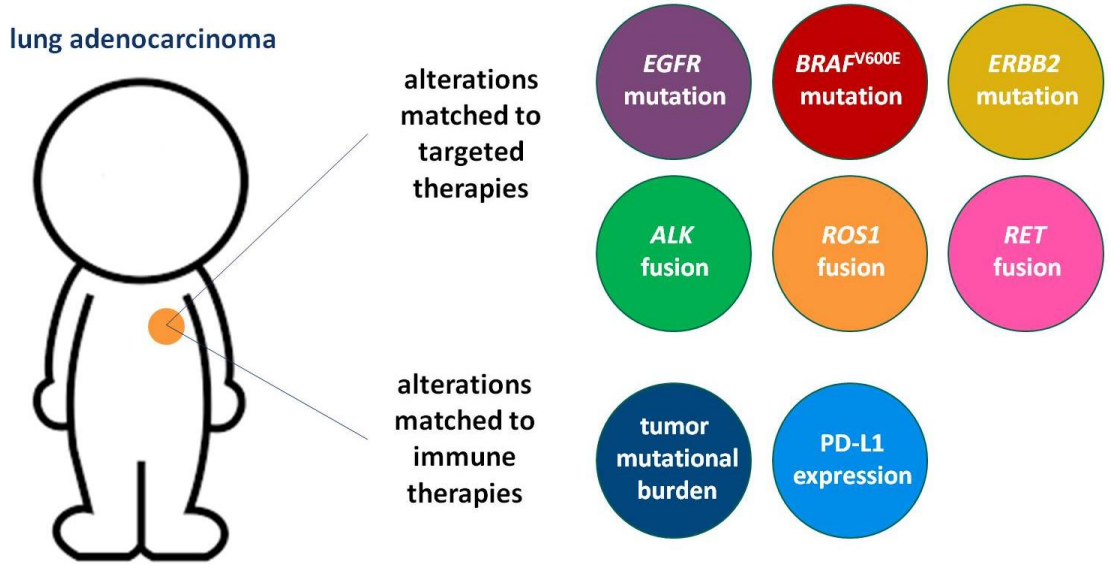
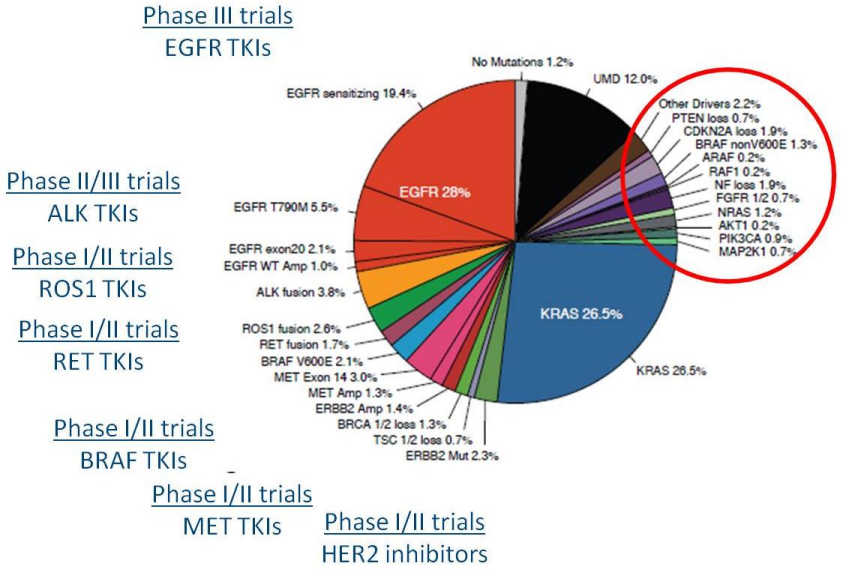
Cancers Can Harbor a Variety of Potentially Actionable Signatures



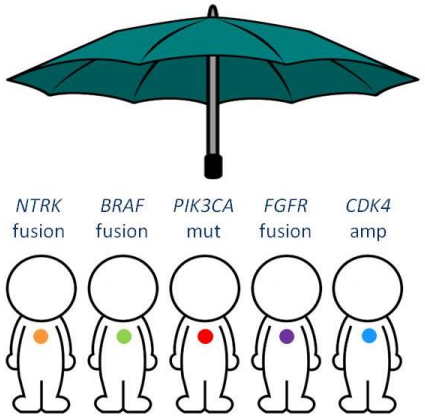
Drilon A. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

It Is Getting More Difficult to Explore Rarer Signatures in One Cancer



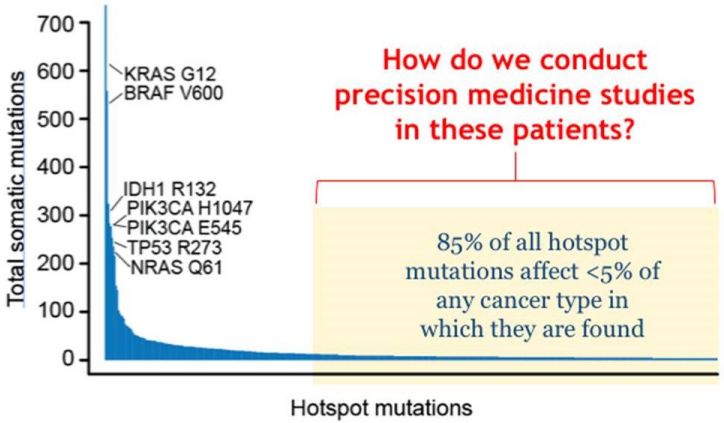
UMBRELLA TRIAL

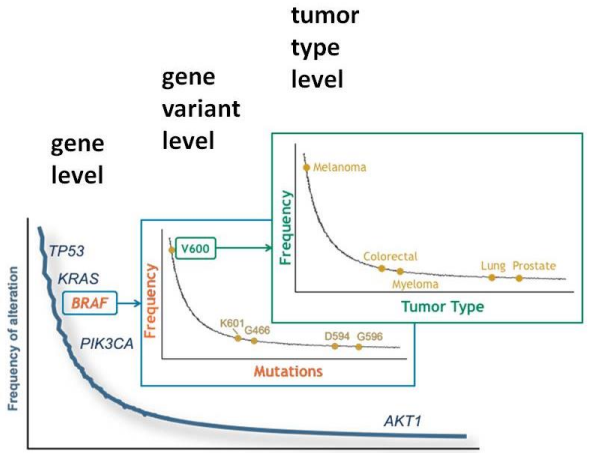
- Multiple qualifying alterations
- Single histology



Jordan EJ, et al. *Cancer Discov*. 2017;7(6):596-609. Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

There Is a "Long Tail" of Hotspot Mutations across Different Cancers





Chang MT, et al. *Nat Biotechnol*. 2016;34(2):155-163. Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

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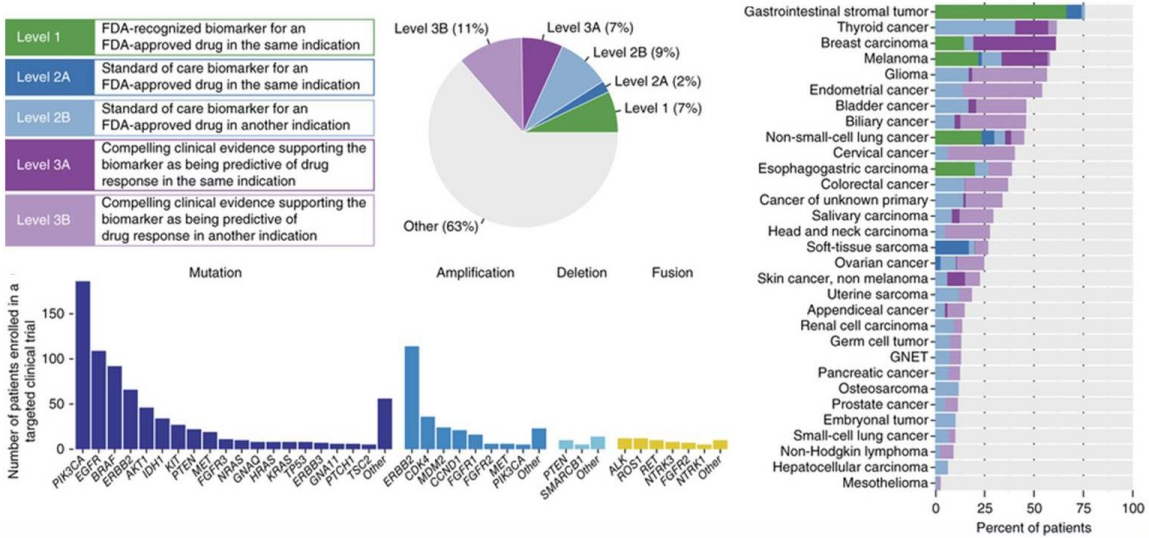
Actionable Alterations Can Be Detected across Cancers in the Clinic

10,000 clinical samples of advanced solid tumors profiled by MSK-IMPACT next-gen sequencing

matched therapies identified



GNET = gastrointestinal neuroectodermal tumor.

Zehir A, et al. *Nat Med*. 2017;23(6):703-713. Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

Tumor-Agnostic Drug Development Can Address the "Long Tail"

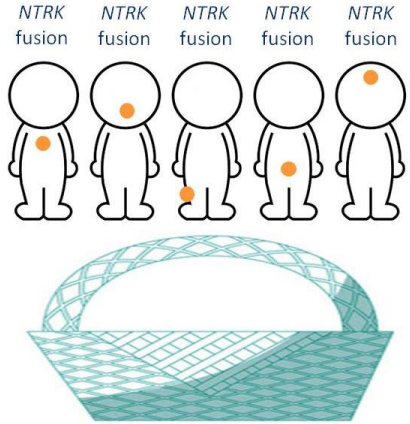
Histology-specific drug development

- Traditional designs
- Umbrella trials

Alteration-specific drug development (agnostic of tumor type)

BASKET TRIAL

- One qualifying group of alterations
- Tumor agnostic patient accrual



Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

A Spectrum of Master Protocols Exists

UMBRELLA TRIAL
- Multiple qualifying alterations
- Single histology

MULTIPLE BASKET TRIALS
- Multiple groups of qualifying alterations
- Histology-agnostic accrual

BASKET TRIAL
- One group of qualifying alterations
- Histology-agnostic accrual

LUNG-MAP
BATTLE

ASCO TAPUR
NCI-MATCH
My Pathway
Signature

Larotrectinib (*NTRK* fusions)
Vemurafenib (*BRAF* mutations)
Neratinib (*HER2* mutations)

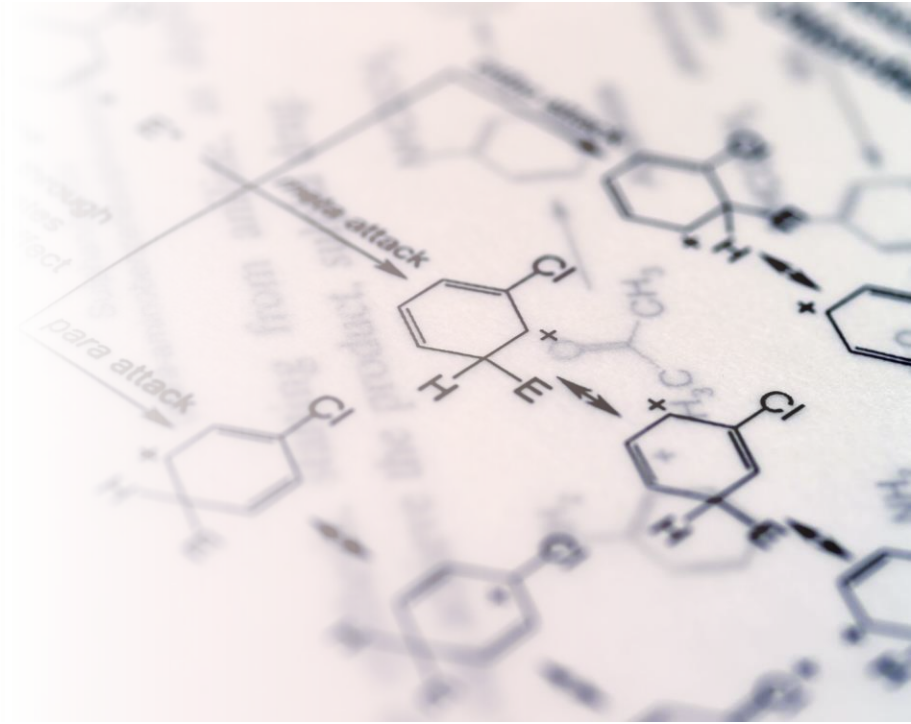
Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

Tumor-Agnostic Examples

Agenda

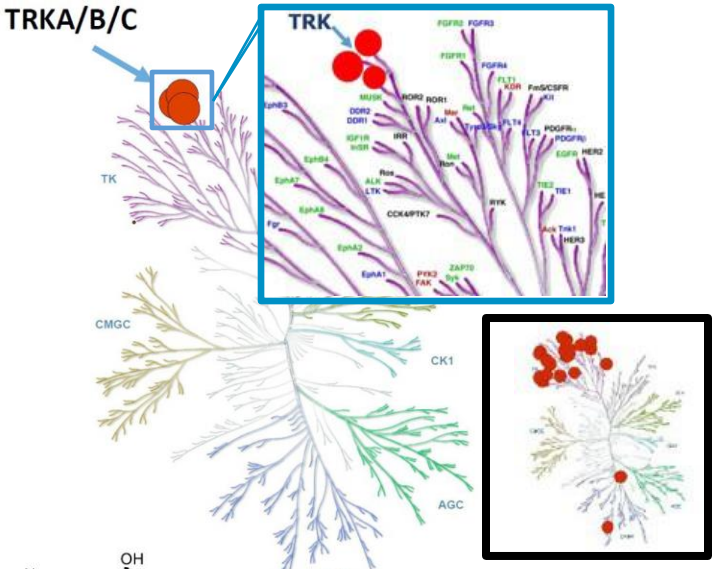
- Emergence of tumor-agnostic therapy

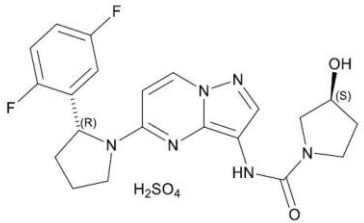
- 3 examples
  - Larotrectinib
  - Dabarafenib and tremetinib
  - Trastuzumab deruxtecan (T-DXd)



Larotrectinib Is a Highly Selective TRK Inhibitor

- First and only selective TRK inhibitor
- High potency against TRKA, TRKB, and TRKC
  - IC_{50} = 5-11 nM in cellular assays
- Slow dissociation; inhibitor stays bound to target
  - T1/2: 160 min
- High selectivity
  - Limited inhibition of other kinases
  - ≥100-fold selectivity versus 229/other kinases





TRKA/B/C = tropomyosin receptor kinase A/B/C.

Hyman DM, et al. *J Clin Oncol*. 2017;35:LBA2501. Drilon A, et al. *N Engl J Med*. 2018;378(8):731-739.

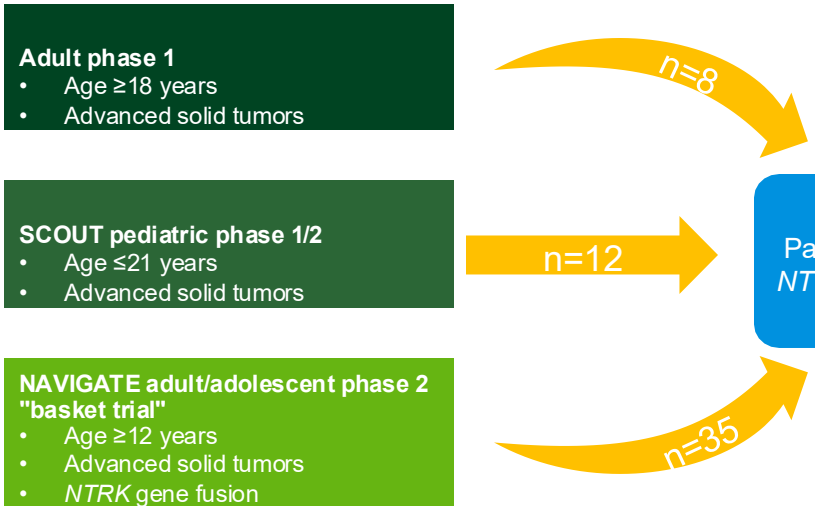
ORIGINAL ARTICLE

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

Drilon A, et al. *N Engl J Med*. 2018;378(8):731-739.

A Pooled Analysis from Three Larotrectinib Clinical Trials Was Performed



TRK fusion status
- Determined by local CLIA (or similarly accredited) laboratories
- Assessed by NGS (n=50) and FISH (n=5) in 15 laboratories*

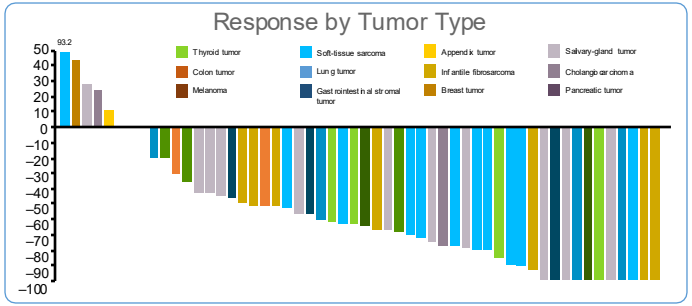
Primary endpoint (combined analysis)
- Overall response rate (ORR)†

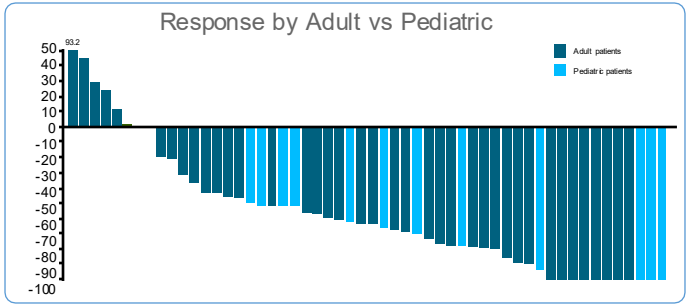
Secondary endpoints
- ORR‡
- Duration of response
- PFS
- Safety (CTCAE 4.0)

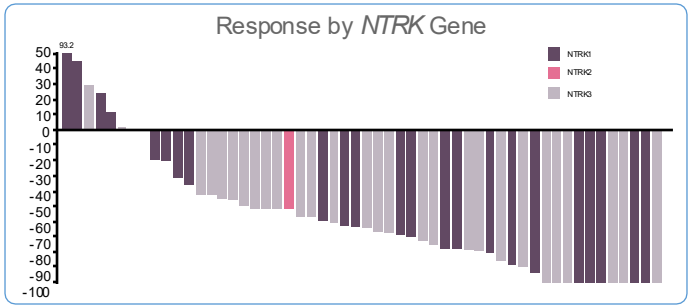
Dosing
- Adults: 100 mg BID
- Children with BSA <1 m^2: 100 mg/m^2 BID
- Treatment beyond progression is permitted if patient continues to benefit

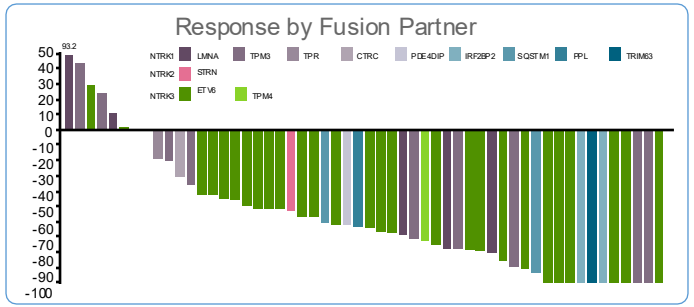
***Confirmation testing was not required or routinely performed. †Assessed by independent radiology review according to RECIST 1.1. ‡According to investigator's assessment. Tumor assessments were performed at baseline and every 8 weeks for 1 year and every 12 weeks thereafter until disease progression.**
BSA = body surface area; CLIA = Clinical Laboratory Improvement Amendments; CTCAE = Common Terminology Criteria for Adverse Events; FISH = fluorescence in situ hybridization; NGS = next-generation sequencing; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumors.
Hyman DM, et al. *J Clin Oncol*. 2017;35:LBA2501. Drilon A, et al. *N Engl J Med*. 2018;378(8):731-739.

Efficacy across Tumor Type, Age, NTRK Gene, or Fusion Partner









Drilon A, et al. *N Engl J Med*. 2018;378(8):731-739.

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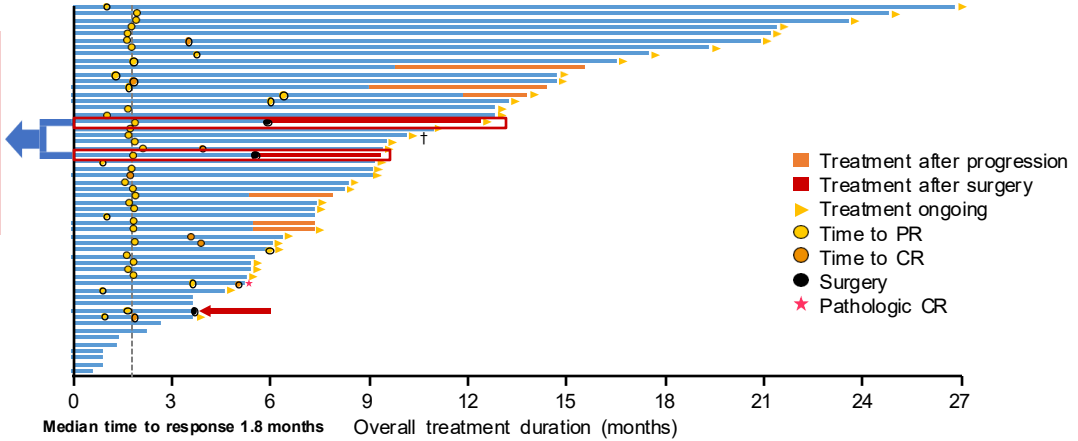
Early and Durable Responses

The median time to response was 1.8 months (range 0.9-6.4), coinciding with the first protocol-mandated response assessment at 8 weeks.

Two pediatric patients with locally advanced IFS had sufficient tumor shrinkage on treatment to allow limb-sparing surgery with curative intent.



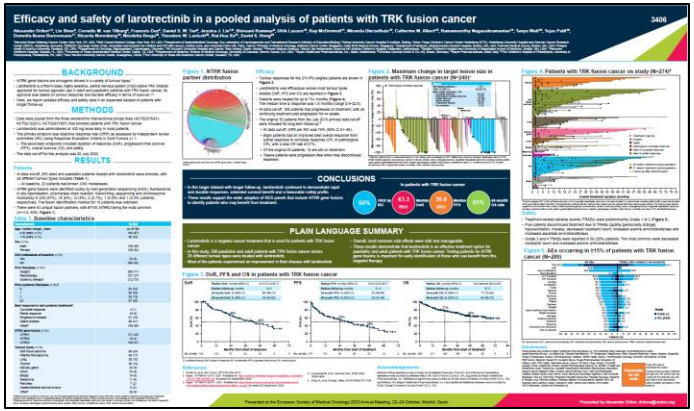
†Patient had a missing restaging scan after the confirmed response was established; PFS was censored at 3.7 months.
IFS = infantile fibrosarcoma; PR = partial response; CR = complete response.
Drilon A, et al. *N Engl J Med*. 2018(8);378:731-739.

A Series of Firsts…

- First FDA breakthrough designation for adults and pediatrics
- First FDA breakthrough designation for a genetic definition of cancer
- First FDA orphan designation for a genetic definition of cancer
- First real-time development of resistance mutation targeted salvage therapy

US Food and Drug Administration (FDA) [www.fda.gov]. Last updated Deember 14, 2018. https://www.fda.gov/drugs/fda-approves-larotrectinib-solid-tumors-ntrk-gene-fusions-0. Cancer Health [www.cancerhealth.com]. Last updated November 26, 2018. https://www.cancerhealth.com/article/fda-vitrakvi-larotrectinib. FDA [www.fda.gov]. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=578317. Drilon A, et al. Cancer Discov. 2017;7(9):963-972.

Efficacy and Safety of Larotrectinib in a Pooled Analysis of Patients with TRK Fusion Cancer



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Drilon A, et al. Presented at: European Society for Medical Oncology (ESMO) 2023 Annual Meeting; October 20-24, 2023; Madrid, Spain. Abstract 3406.

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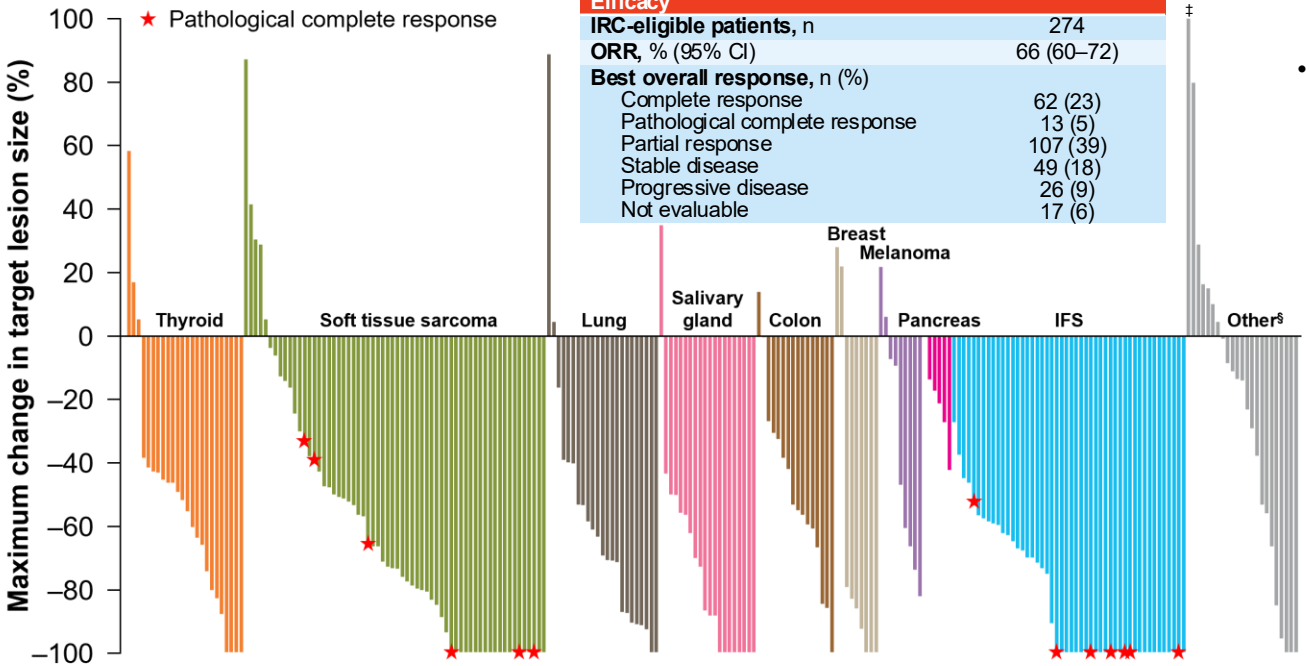
Efficacy

Maximum change in target lesion size in patients with TRK fusion cancer (n=240)†

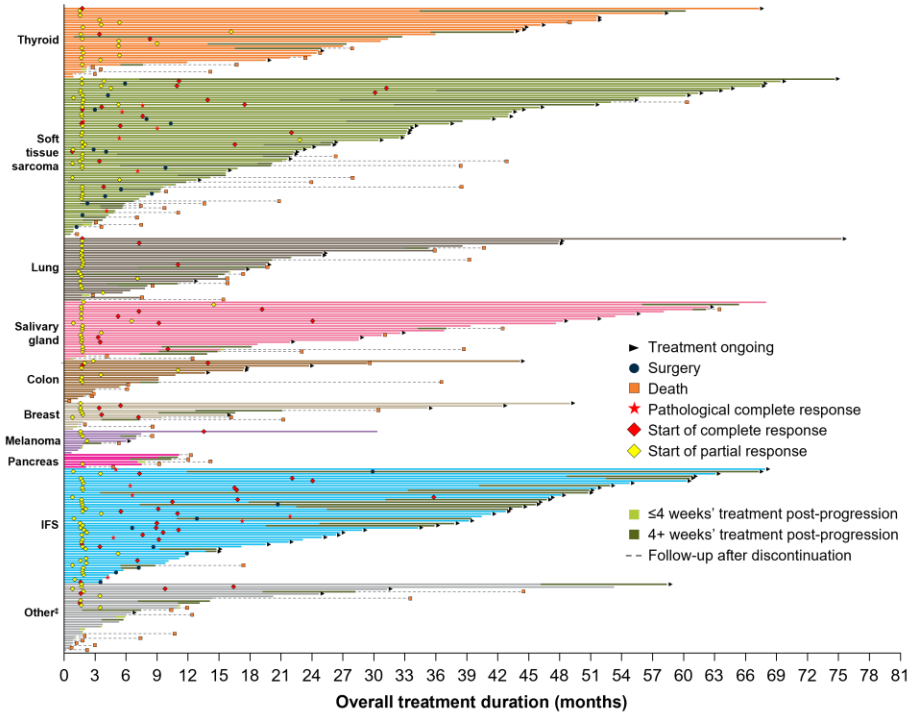


Efficacy	
IRC-eligible patients, n	274
ORR, % (95% CI)	66 (60–72)
Best overall response, n (%)	
Complete response	62 (23)
Pathological complete response	13 (5)
Partial response	107 (39)
Stable disease	49 (18)
Progressive disease	26 (9)
Not evaluable	17 (6)

- Larotrectinib was efficacious across most tumor types
- The original 55 patients from the July 2018 primary data cutoff were included for long-term follow-up.
  - At data cutoff, ORR per IRC was 75% (95% CI 61-85)
  - Eight patients had an improved best overall response from partial response to complete response (or pathological complete response), with a total complete response rate of 27%
  - Of the original 55 patients, 10 are still on treatment
  - Twelve patients were progression-free when they discontinued treatment

†Thirty-four patients had no measurable lesions or had missing data as assessed by IRC. ‡Patient had a maximum charge in target lesion size of +277%. §Other includes appendix, bone sarcoma, cancer of unknown primary, cervix, cholangiocarcinoma, congenital mesoblastic nephroma, duodenal, external auditory canal, gastric, gastrointestinal stromal tumor, hepatic, esophageal, prostate, rectal, thymus, urothelial, and uterus.
IRC = independent review committee.
Drilon A, et al. Presented at: ESMO 2023 Annual Meeting; October 20-24, 2023; Madrid, Spain. Abstract 3406.

Patients with TRK Fusion Cancer on Study (N=274)†



- Patients were treated for up to 75+ months
- The median time to response was 1.8 months (range 0.9-22.9)
- At data cutoff, 108 patients had progressed on treatment, with 46 continuing treatment post-progression for ≥4 weeks

†Forty-six patients (IFS: n=28; soft tissue sarcoma: n=16; congenital mesoblastic nephroma: n=2) were enrolled in a "wait-and-see" analysis (patients with a response are taken off drug and still enrolled in the trial). This included four patients with two "wait-and-see" periods and two patients with three "wait-and-see" periods. The "wait-and-see" periods ranged from 0.9 months to 68+ months. ‡Other includes appendix, bone sarcoma, cancer of unknown primary, cervix, cholangiocarcinoma, congenital mesoblastic nephroma, duodenal, external auditory canal, gastric, gastrointestinal stromal tumor, hepatic, esophageal, prostate, rectal, thymus, urothelial, and uterus.

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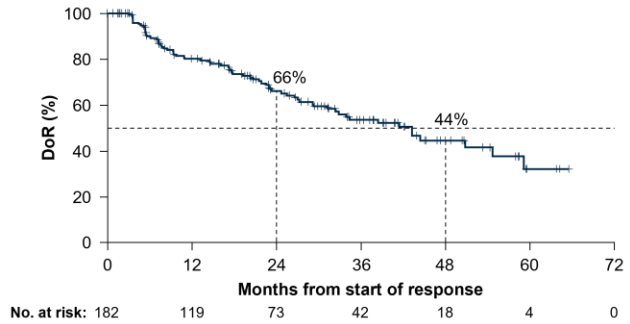
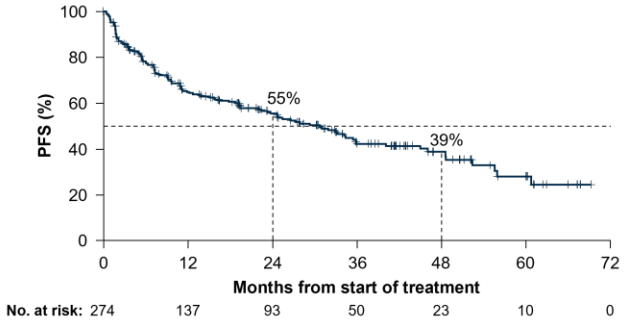
DoR, PFS, and OS in Patients with TRK Fusion Cancer

DoR



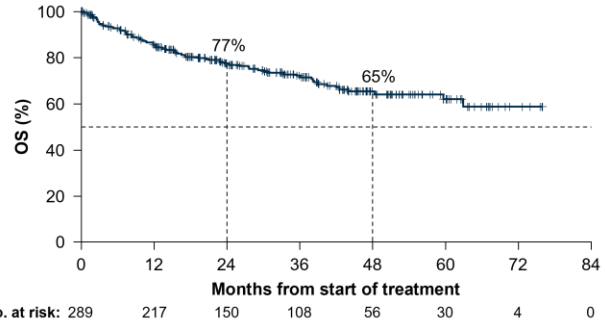
Median DoR, months (95% CI)	43.3 (31.4-54.7)
Median follow-up, months	31.5
24-month DoR, % (95% CI)	66 (58-74)
48-month DoR, % (95% CI)	44 (34-55)

PFS



Median PFS, months (95% CI)	30.8 (22.5-36.1)
Median follow-up, months	31.3
24-month PFS, % (95% CI)	55 (49-62)
48-month PFS, % (95% CI)	39 (31-46)

OS

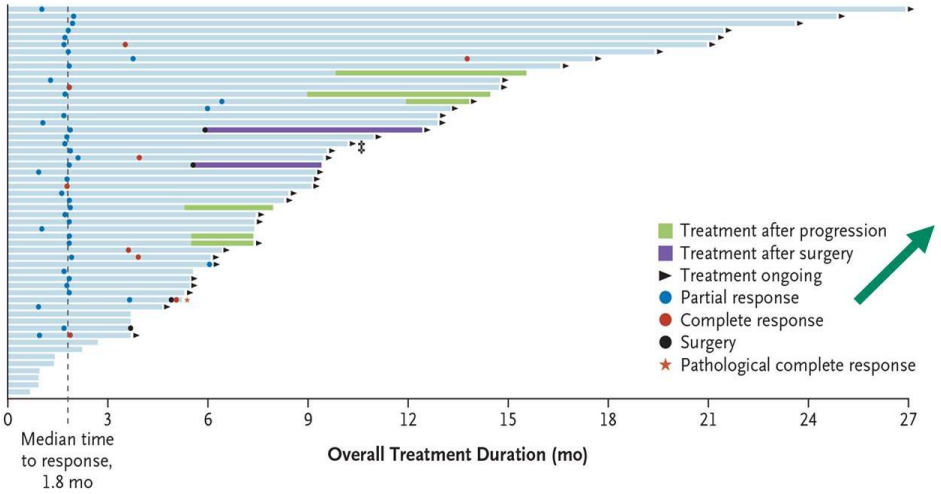


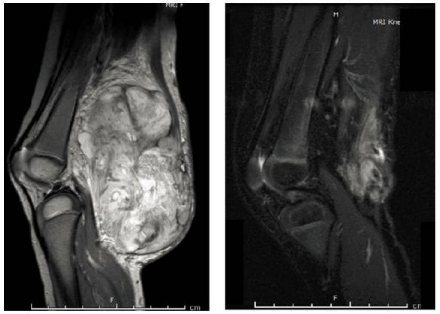
Median OS, months (95% CI)	NR (63.4-NE)
Median follow-up, months	37.2
24-month OS, % (95% CI)	77 (72-83)
48-month OS, % (95% CI)	65 (58-72)

DoR = duration of response; NE = not estimable; NR = not reached; OS = overall survival.

Drilon A, et al. Presented at: ESMO 2023 Annual Meeting; October 20-24, 2023; Madrid, Spain. Abstract 3406.

Larotrectinib Trial Uncovers the Potential for Neoadjuvant Therapy





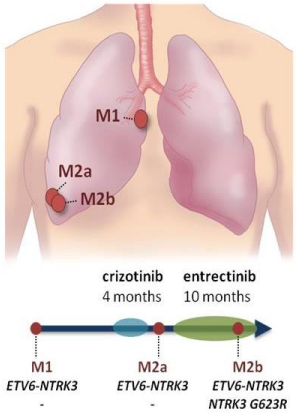
2 year-old requiring leg amputation for TRK fusion-positive sarcoma

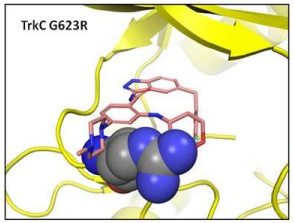
- dramatic response to larotrectinib
- underwent limb-sparing surgery with no functional deficits
- pathologic complete response

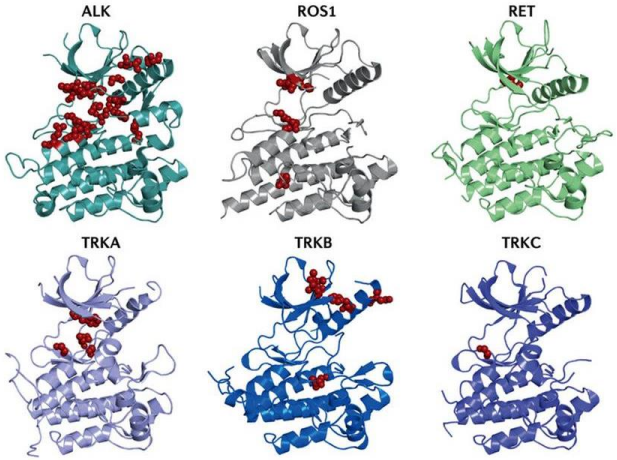
Drilon A, et al. *N Engl J Med*. 2018;378(8):731-739. Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

Basket Trials Serve as Platforms to Understand Resistance

novel acquired resistance solvent front mutation identified on entrectinib trial



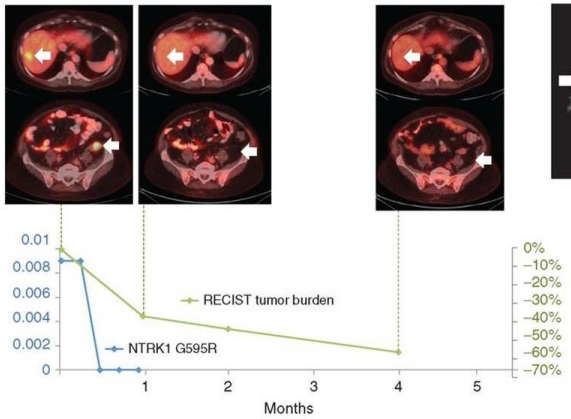


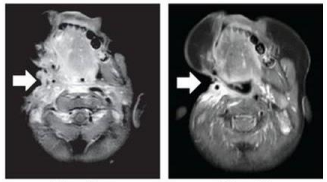


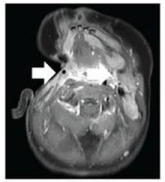
Drilon A, et al. *Ann Oncol*. 2016;27(5):920-926. Schram AM, et al. *Nat Rev Clin Oncol*. 2017;14(12):735-748. Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

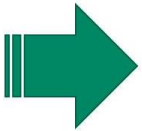
Basket Trials Serve as Platforms to Understand Resistance

adult and pediatric patients with solvent front-mediated resistance respond to next-generation TKI on compassionate use trials









next-generation TKI now in phase I/II clinical trial testing

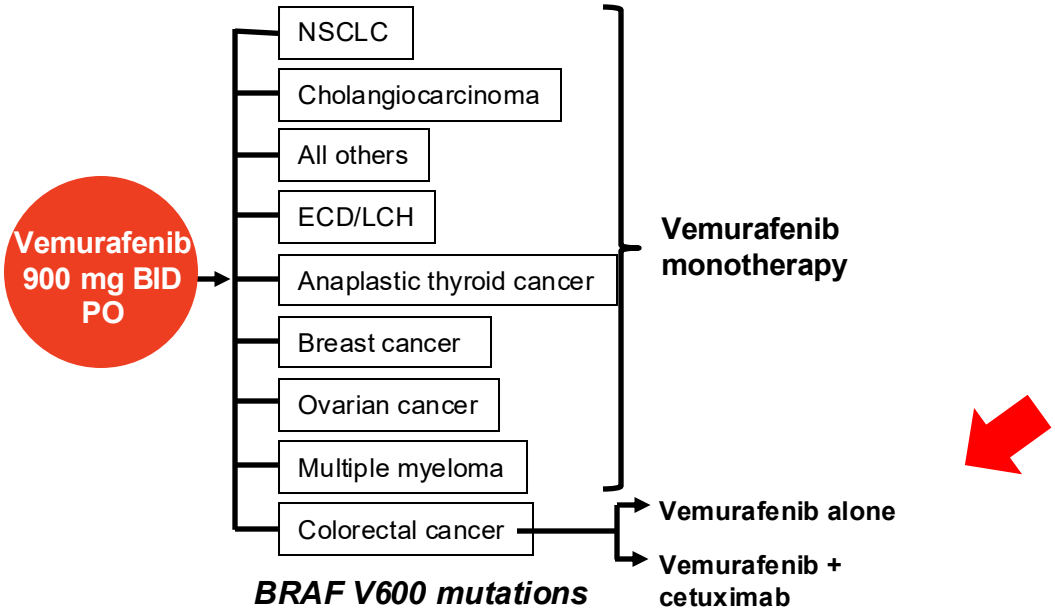
Drilon A, et al. *Cancer Discov*. 2017;7(9):963-972. Drilon A. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago, Illinois. Slide courtesy of Drilon A.

BRAF in Cancer

- BRAFmut oncogene—5-10% of all human malignancies; most of the tumors that **express BRAF V600E mutations are rare or ultra-rare cancers.**
- Constitutive activation of the MAPK pathway; most common mutation of BRAF valine-to-glutamic acid substitution at codon 600 (V600E)
- Driver mutation in
  - Solid tumors such as melanoma, colorectal cancer, papillary thyroid cancer, NSCLC, ovarian cancer, and GIST, etc.
  - Hematological **malignanices**: Langerhans cell histiocytosis, Erdheim-Chester disease, hairy cell leukemia, etc

Morris V, Kopetz S. *F1000Prime Rep*. 2013;5:11. Subbiah V, et al. *Nat Med*. 2023;29(5):1103-1112. Haroche J, et al. *Blood*. 2012;120(13):2700-2703. Slide courtesy of Subbiah V.

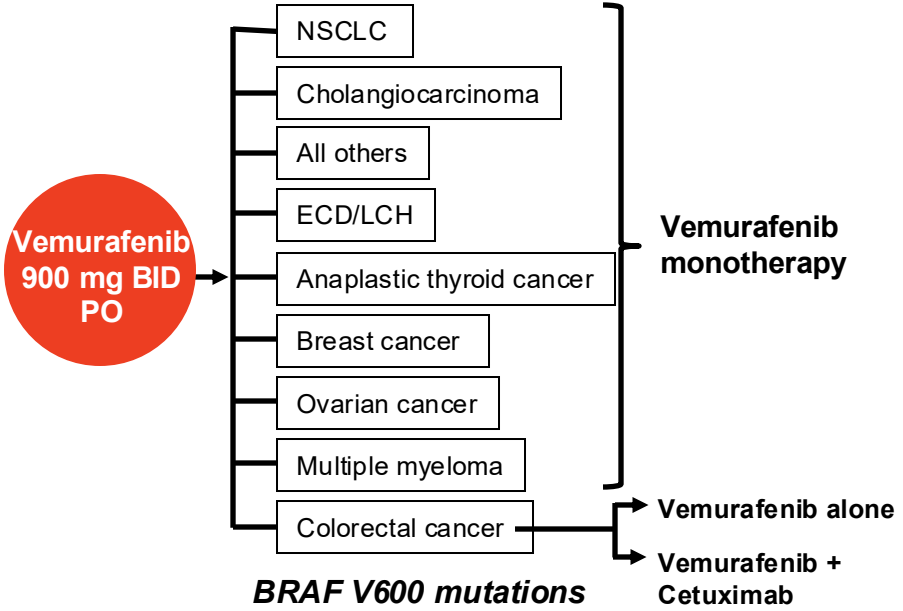
Vemurafenib Basket Trial



ECD = Erdheim-Chester disease; LCH = Langerhans cell histiocytosis.

Hyman DM, et al. *N Engl J Med*. 2015;373(8):726-736. Slide courtesy of Subbiah V.

Vemurafenib Basket Trial

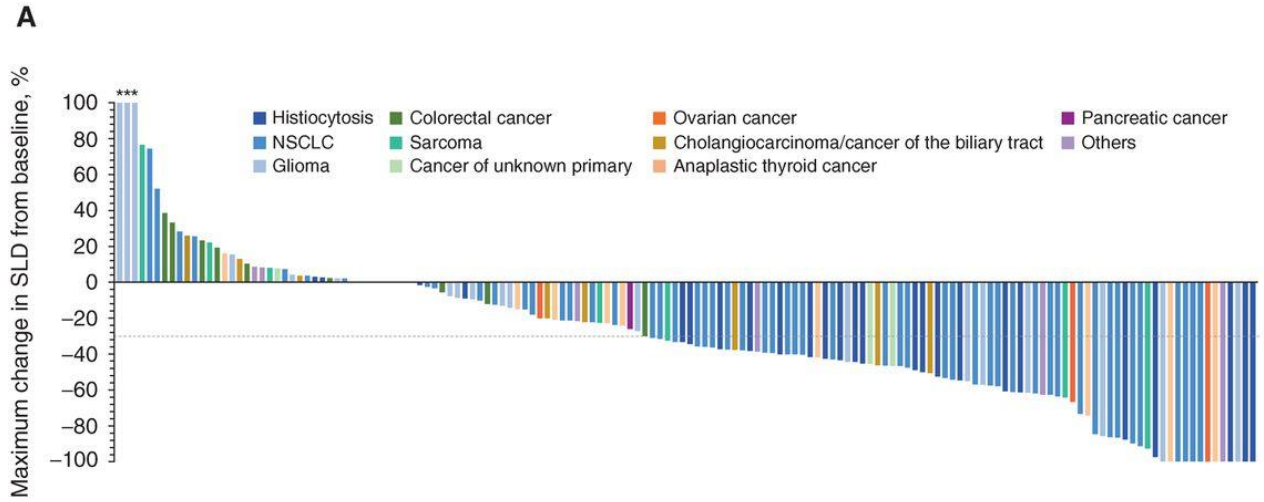


- In NSCLC, the response rate was 42%
- In Erdheim-Chester disease or Langerhans'-cell histiocytosis, the response rate was 43% (FDA approval)
- Responses in pleomorphic xanthoastrocytoma, anaplastic thyroid cancer, cholangiocarcinoma, salivary-duct cancer, ovarian cancer, and clear-cell sarcoma
- Among patients with colorectal cancer who received vemurafenib and cetuximab
- Validated BRAF V600 as a therapeutic target beyond melanoma
- Lead to tumor-agnostic sensitivity to vemurafenib with the exception of colorectal cancer

Hyman DM, et al. *N Engl J Med*. 2015;373(8):726-736. Slide courtesy of Subbiah V.

Pan-Cancer Activity of Vemurafenib in BRAF V600-Positive Non-Melanoma Cancers

Were there pre-clinical BRAF+ models across multiple tumor types?

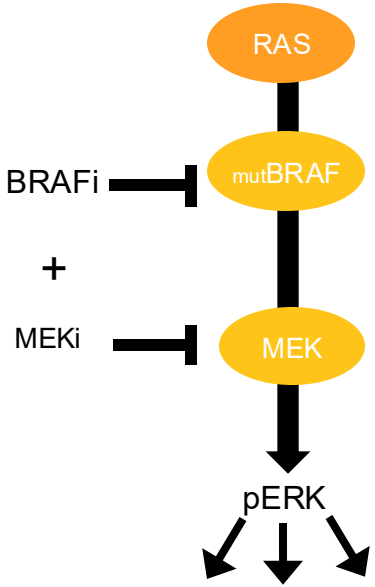


Subbiah V, et al. *Cancer Discov*. 2020;10(5):657-663. Slide courtesy of Subbiah V.

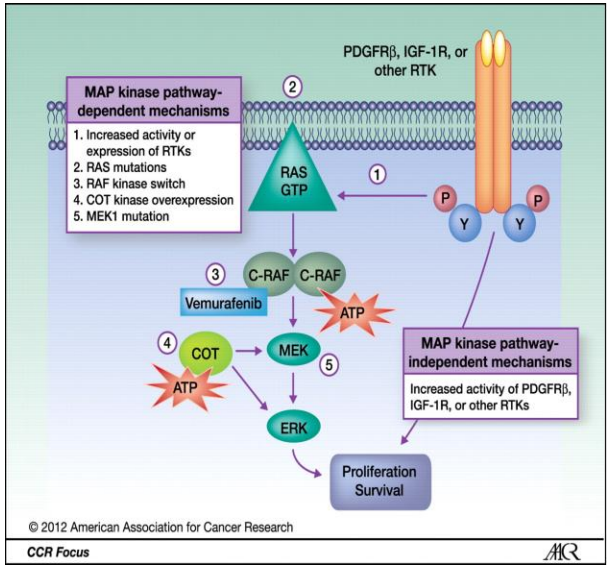
Great Debates Solid Tumors

Rationale for the RAF/MEK Combination

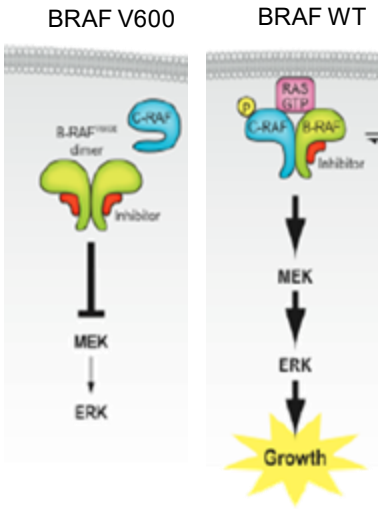
Sustained target inhibition to observe more prolonged and durable anti-tumor effect



Delay and potentially prevent the development of resistance



Prevent/delay hyperproliferative lesions and secondary malignancies



BRAFi = BRAF inhibitor; MEKi = MEK inhibitor.
Slide courtesy of Subbiah V.

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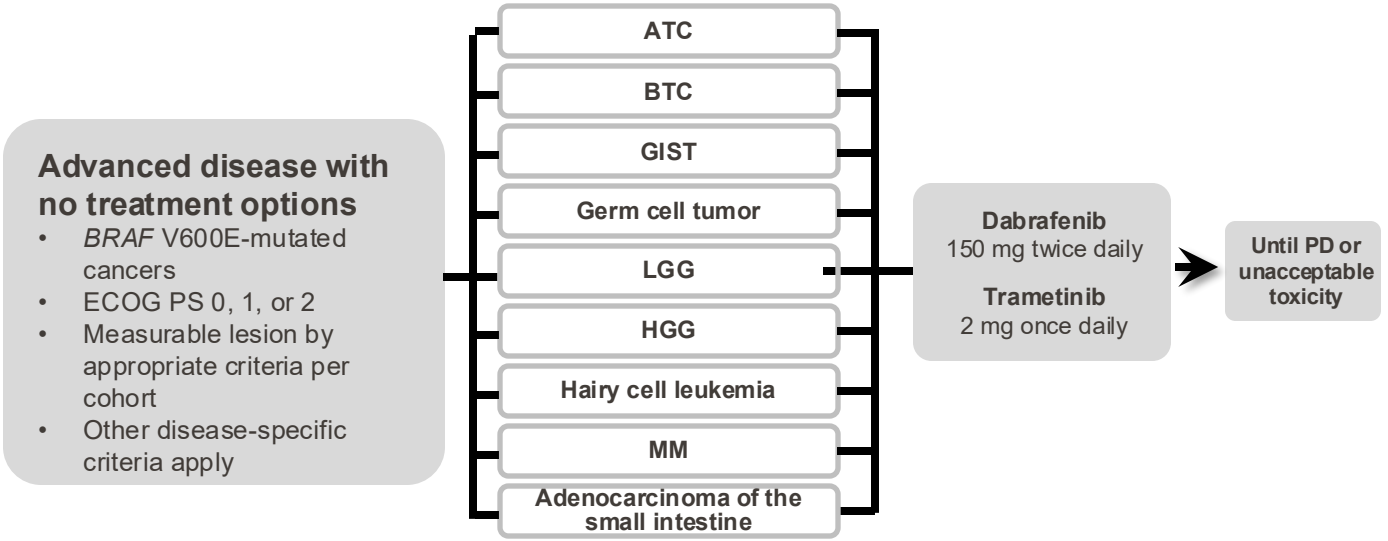
ROAR Study Design = Rare Oncology-Agnostic Research



Primary endpoint: Investigator assessed ORR

Secondary endpoints: DOR, PFS, OS, safety

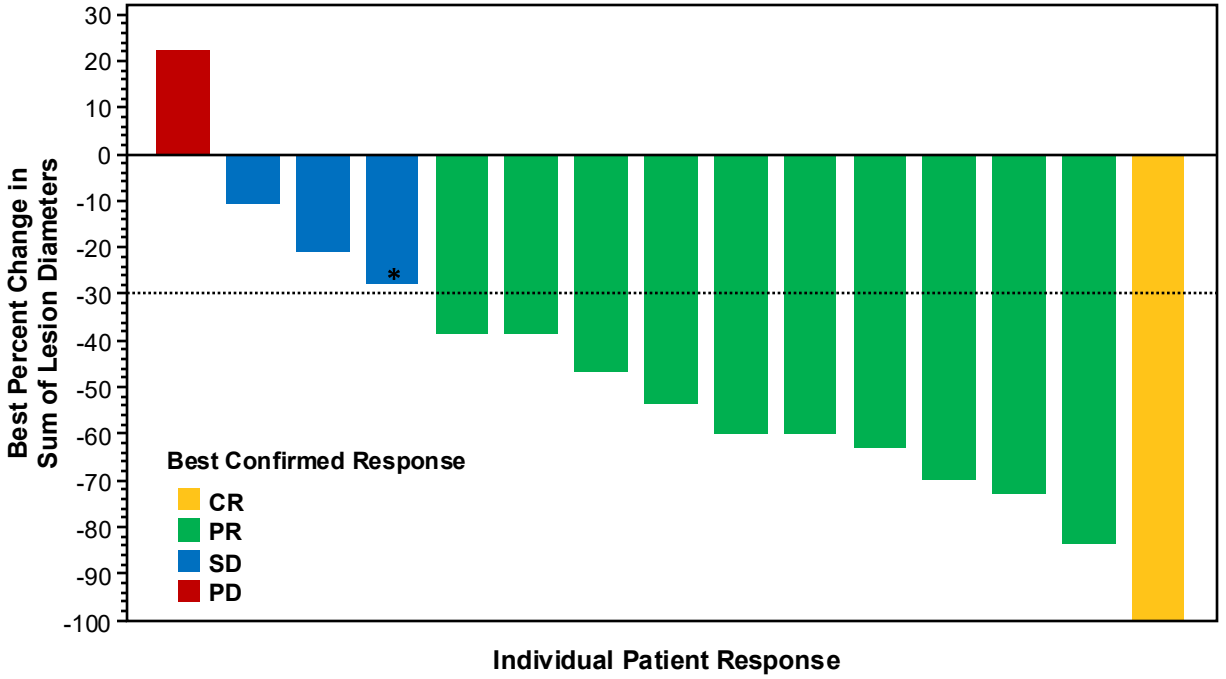
Other endpoints: Exploratory biomarkers, changes from baseline in HRQOL

ECOG PS = Eastern Cooperative Oncology Group performance status; ATC = anaplastic thyroid carcinoma; BTC = biliary tract cancer; LGG = low-grade glioma; HGG = high-grade glioma; MM = multiple myeloma; PD = progressive disease; HRQOL = health-related quality of life.

Subbiah V, et al *J Clin Oncol*. 2016;34(15 Suppl):TPS2604. Slide courtesy of Subbiah V.

Anaplastic Thyroid Cancer BRAF V600+

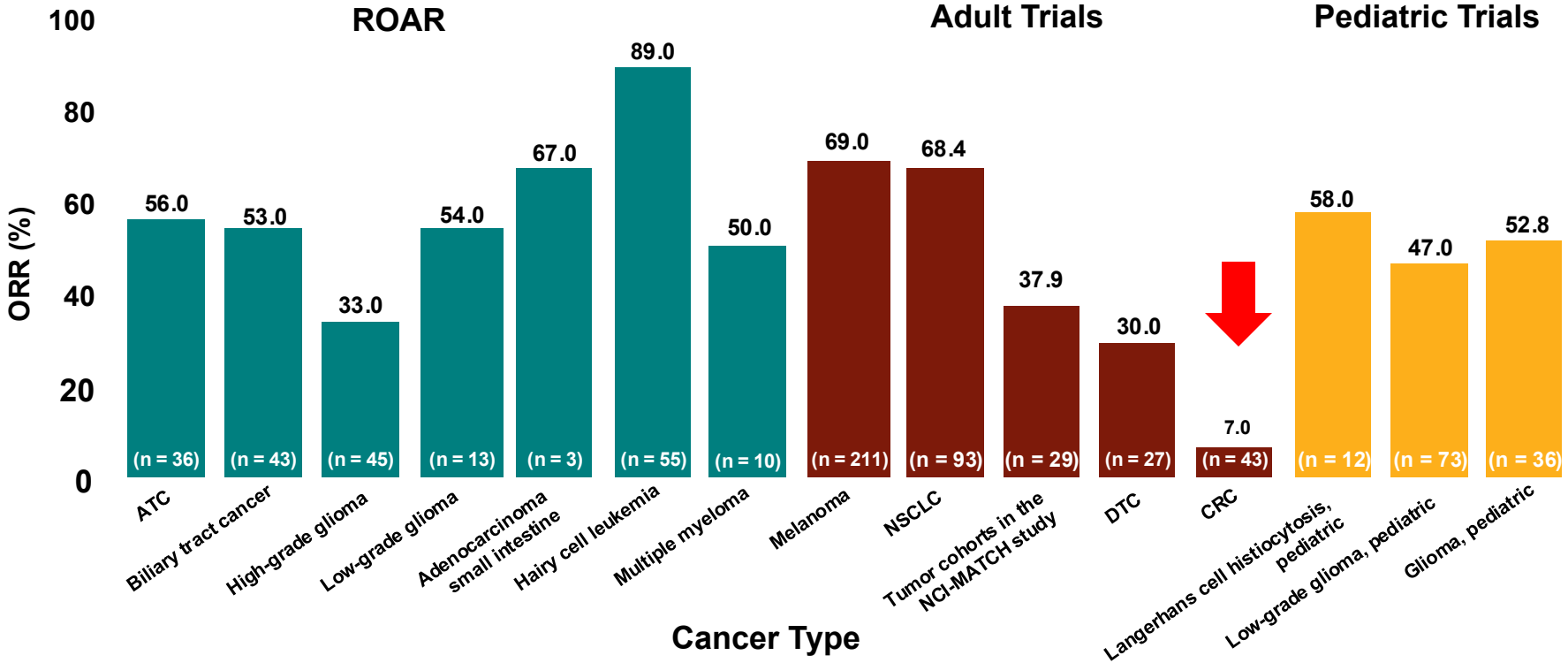
69% ORR



SD = stable disease.

Subbiah V, et al. *J Clin Oncol.* 2018;36(1):7-13. Slide courtesy of Subbiah V.

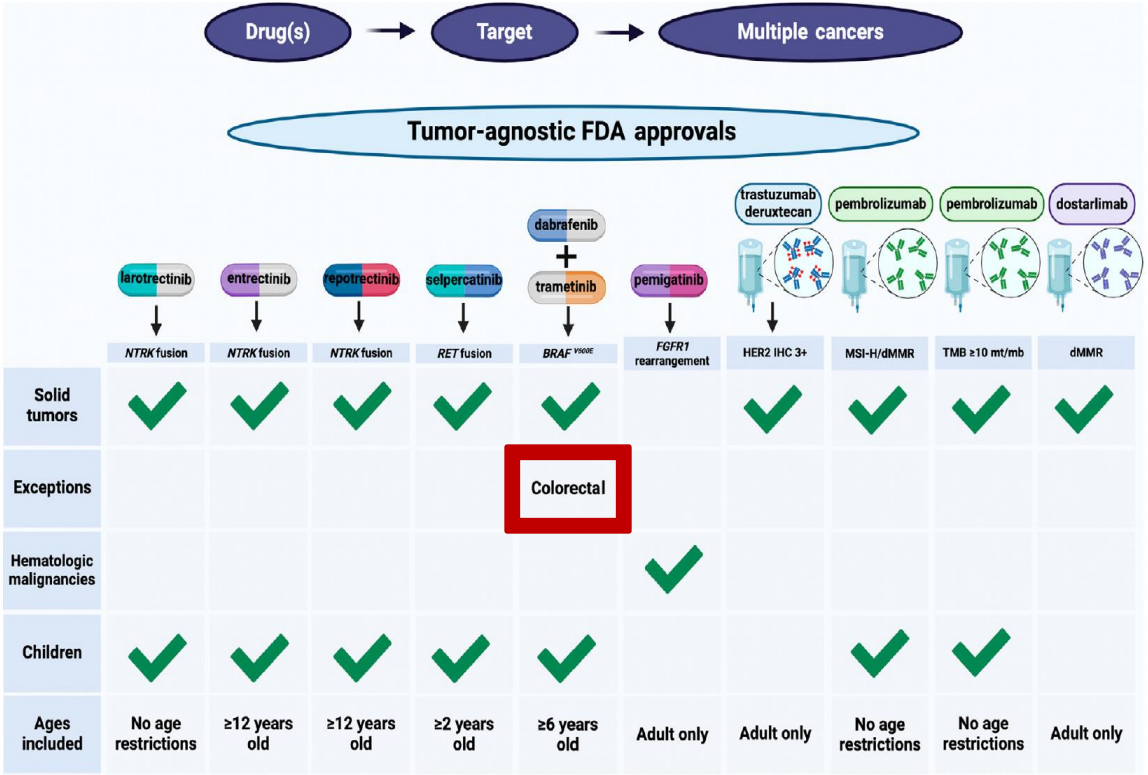
Response Rates with Dabrafenib + Trametinib across BRAF V600E-Mutated Cancers



DTC = differentiated thyroid cancer.

Subbiah. V Nat Med. 2023;29:1103. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated August 21, 2023.
https://clinicaltrials.gov/study/NCT02034110. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated July 14, 2021.
https://clinicaltrials.gov/study/NCT02124772. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated December 13, 2023.
https://clinicaltrials.gov/study/NCT02684058. Slide courtesy of Subbiah V.

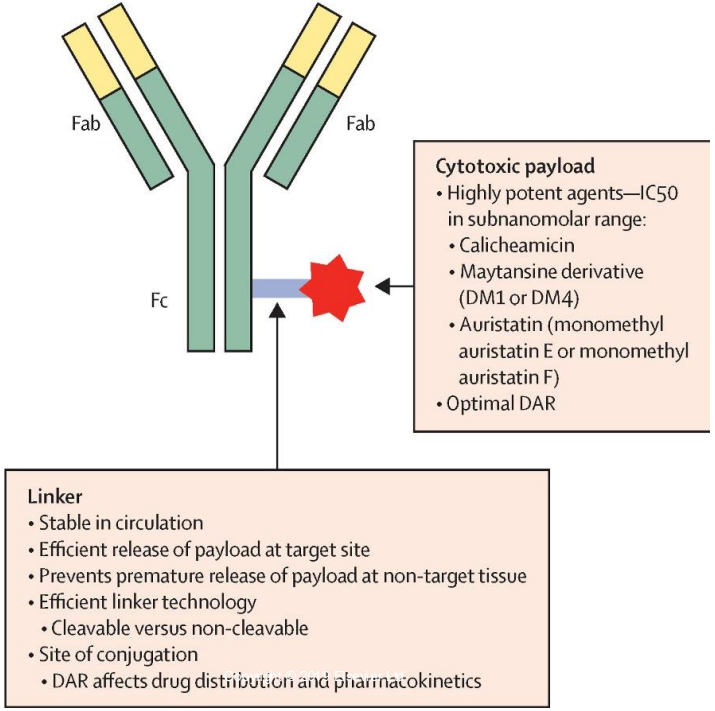
The FDA Allows Exceptions!



Kudek MR, et al. *Trends Cancer*. 2025;11(8):726-735.

Great Debates Solid Tumors

Antibody-Drug Conjugates

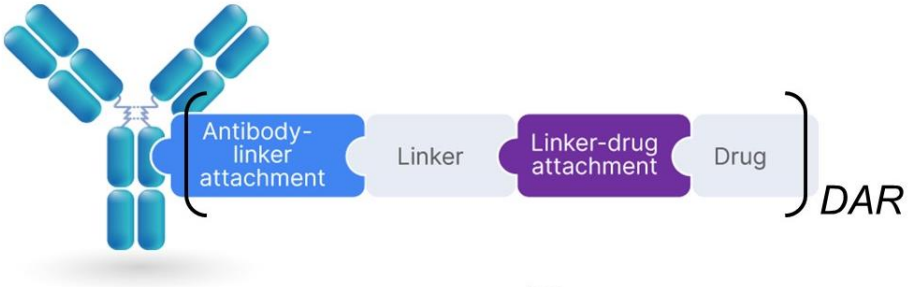


Novel payloads: eg, immune modulators

Increasing emphasis on optimizing drug antibody ratio (DAR)

Chau CH, et al. *Lancet*. 2019;394(10200):793-804. Slide courtesy of Meric-Bernstam F.

More than 400 ADCs Have Entered Clinical Development to Date!



450 ADCs have entered the clinic:

- **13 approved by US FDA**
  +3 additional by China NMPA
  +1 additional by UK MHRA and Japan PMDA
- **271 in clinical development**
- **163 discontinued**

What have we learned from this rich history?

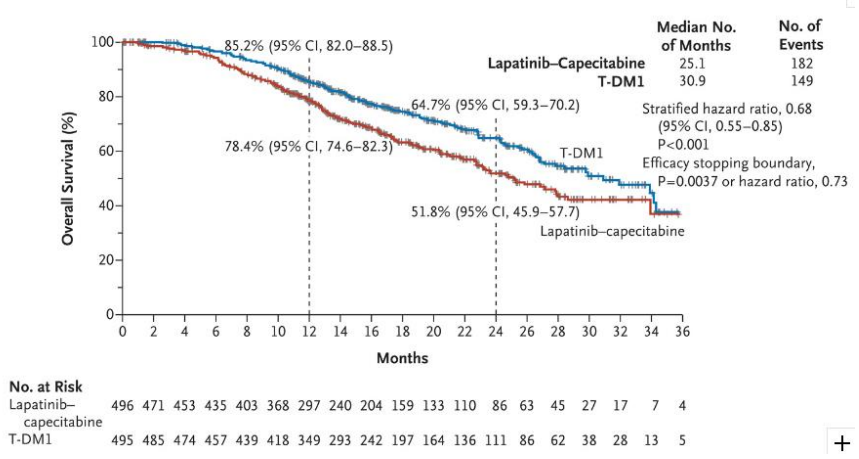
ADCs on file, manually curated, as of 23 May 2025

NMPA = National Medical Products Administration; MHRA = Medicines and Healthcare Products Regulatory Agency; PMDA = Pharmaceuticals and Medical Devices Agency.

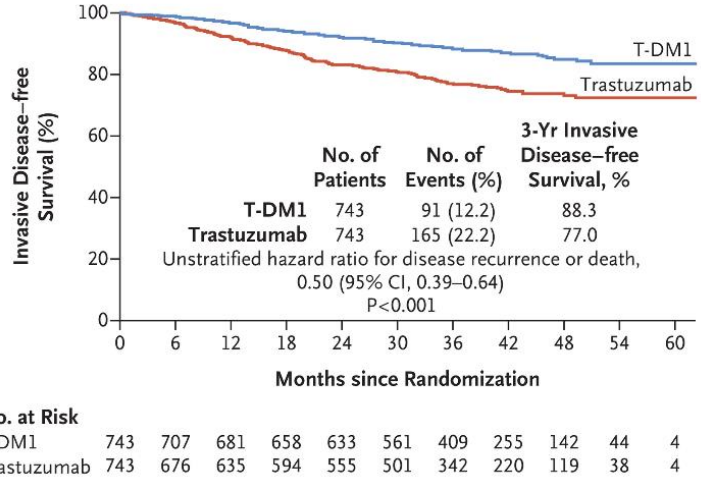
Lorusso PM. Presented at: ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois.

Antibody-Drug Conjugates for Early and Metastatic Disease: Trastuzumab Emtansine (T-DM1) for HER2+ Breast Cancer

EMELIA trial: OS with T-DM1 vs lapatinib-capecitabine HER2+ advanced breast cancer



KATHERINE trial: invasive DFS with adjuvant T-DM1 vs trastuzumab for residual invasive HER2+ breast ca

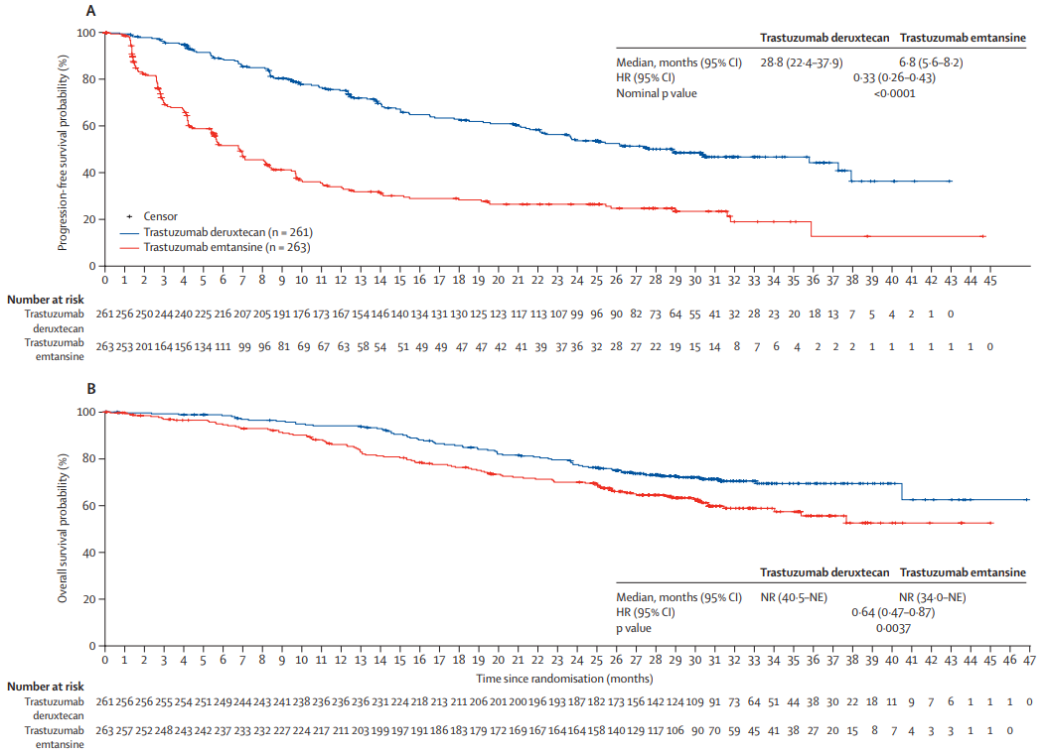


DFS = disease-free survival.

Verma S, et al. *N Engl J Med*. 2012;367(19):1783-1791. Von Minckwitz G, et al. *N Engl J Med*. 2019;380(7):617-628.

Slide courtesy of Meric-Bernstam F.

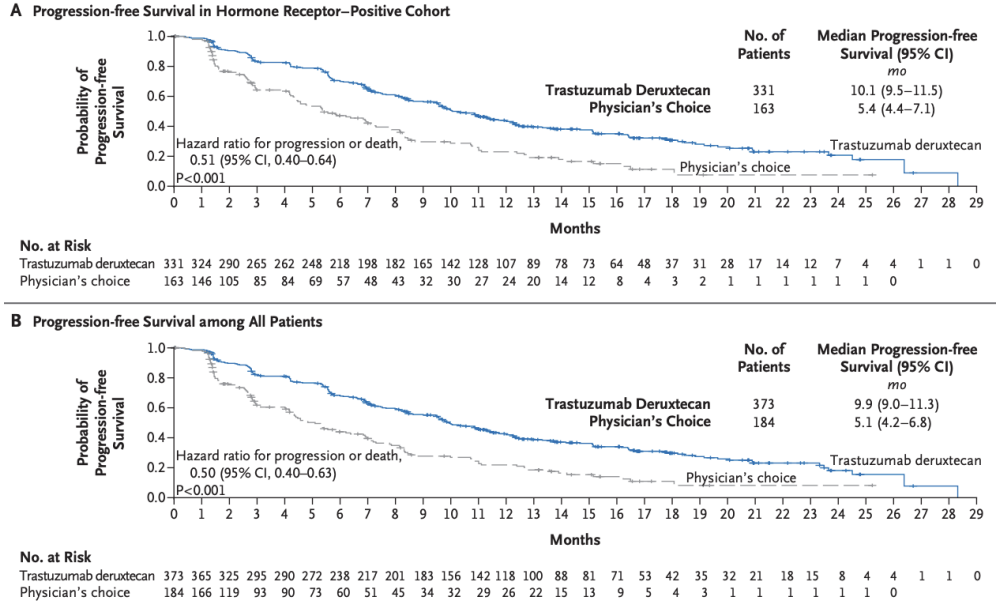
T-DXd versus T-DM1 in HER2+ MBC: DESTINY-Breast03



Hurvitz SA, et al. *Lancet*. 2023;401(10371):105-117. Slide courtesy of Meric-Bernstam F.

Great Debates Solid Tumors

T-DXd Activity in HER2 Low Breast Cancer



DESTINY Breast04
HER2 LOW:
IHC 1+ OR IHC 2+ ISH -

In HR+ cohort, the median PFS
10.1 months for T-DXd
5.4 months for physician's choice
Hazard ratio for disease progression or death, 0.51; *P*<0.001)

OS 23.9 months and 17.5 months, respectively (hazard ratio for death, 0.64; *P*=0.003).

Modi S, et al. *N Engl J Med*. 2022;387(1):9-20. Slide courtesy of Meric-Bernstam F.

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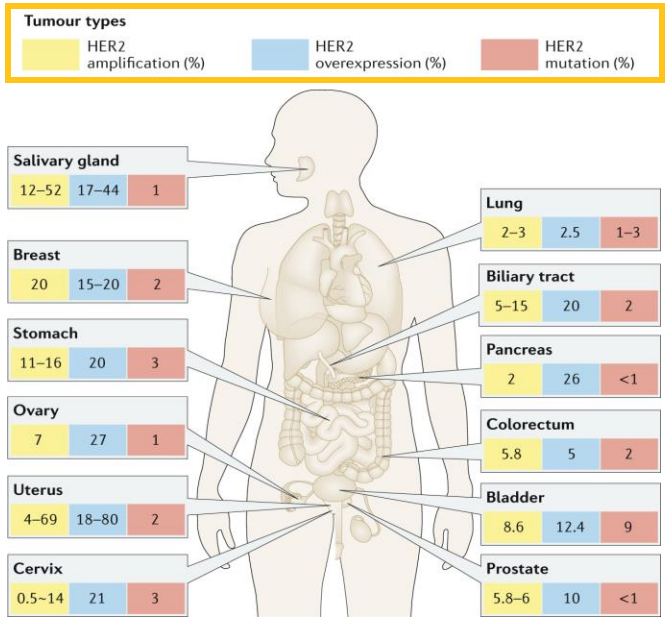
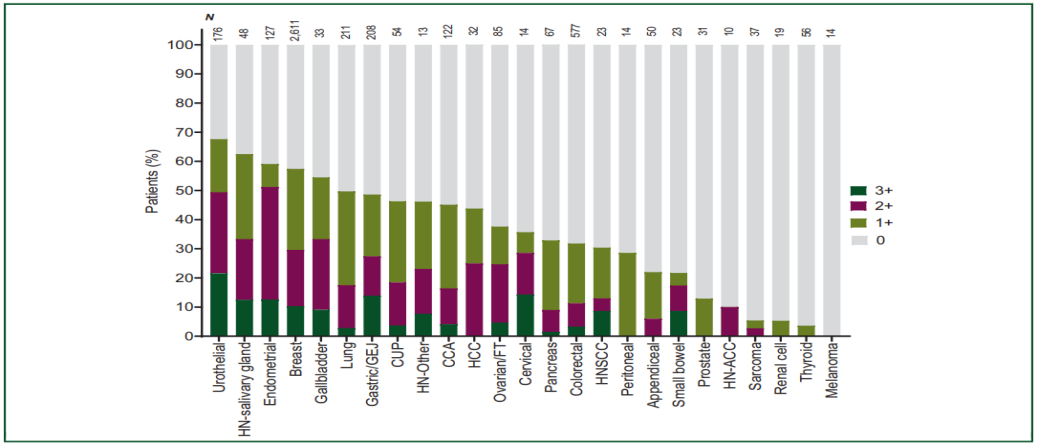
HER2 as an Opportunity in Cancer



Single institution series: 4701 patients underwent HER2 testing: Nearly half (49.8%) had HER2 expression: 8.7% 3+, 16.9% 2+, 24.2% 1+.



Oh DY, et al. *Nat Rev Clin Oncol*. 2020;17(1):33-48. Uzunparmak B, et al. *Ann Oncol*. 2023;34(11):1035-1046.
Slide courtesy of Meric-Bernstam F.

Do ADCs Have Tumor Agnostic Activity for Target Expressors?

DESTINY-PanTumor02: a Phase 2 study of T-DXd for HER2-expressing solid tumors

An open-label, multicenter study (NCT04482309)

Key eligibility criteria

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by anti-HER2 IHC system if local test not feasible (ASCO/CAP gastric cancer scoring[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1

T-DXd
5.4 mg/kg Q3W

40 per cohort[b]

- Endometrial cancer
- Cervical cancer
- Ovarian cancer
- Bladder cancer
- Other tumors[c]
- Biliary tract cancer
- Pancreatic cancer

Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DOR, DCR, PFS, OS
- Safety

Exploratory analysis

- Subgroup analyses by HER2 status

Primary analysis
data cutoff: Jun 8, 2023
Median follow up: 12.75 mo

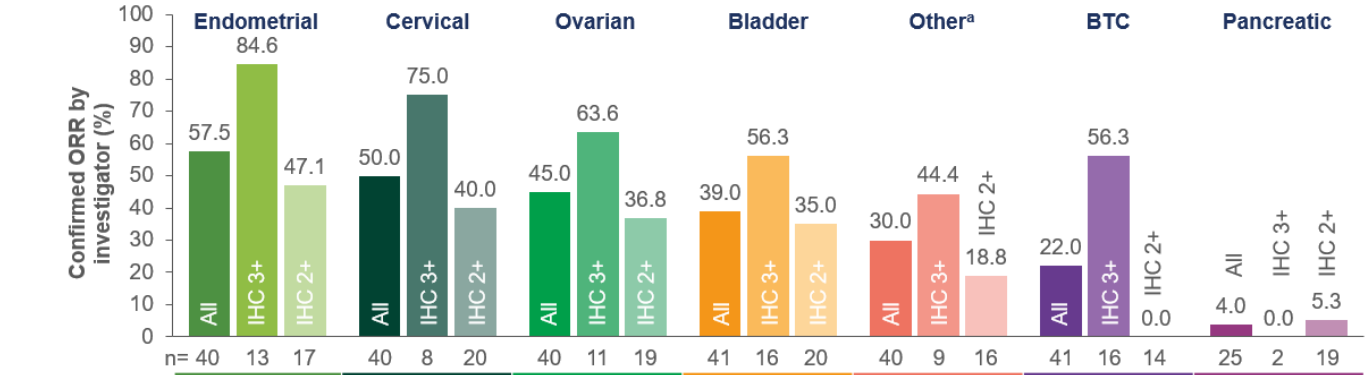
Baseline characteristics

- 267 patients received treatment; 202 (75.7%) based on local HER2 testing
  - 111 (41.6%) patients were IHC 3+ based on HER2 test (local or central) at enrollment, primary efficacy analysis (all patients)
  - **75 (28.1%) patients were IHC 3+ on central testing**, sensitivity analysis on efficacy endpoints (subgroup analyses)
- Median age was 62 years (23–85) and **109 (40.8%) patients had received ≥3 lines of therapy**

[a]Patients were eligible for either test. All patients were centrally confirmed; [b]planned recruitment, cohorts with no objective responses in the first 15 patients were to be closed; [c]patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.
2L = second-line; CAP = College of American Pathologists; DCR = disease control rate; IHC = immunohistochemistry; WHO = World Health Organization.
Hofmann M, et al. *Histopathology*. 2008;52(7):797-805. Slide courtesy of Meric-Bernstam F.

Great Debates Solid Tumors

T-DXd Has Activity across Tumor Types in Patients with HER2 3+ Expression



	All patients (N=267)	IHC 3+ (n=75)	IHC 2+ (n=125)
ORR, % (95% CI)	37.1 (31.3, 43.2)	61.3 (49.4, 72.4)	27.2 (19.6, 35.9)
Median DOR, months (95% CI)[b]	11.3 (9.6, 17.8)	22.1 (9.6, NR)	9.8 (4.3, 12.6)

Analysis of ORR by investigator was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25, IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75 or IHC 2+ (n=125) status. Analysis of DOR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. aResponses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer; bincludes patients with a confirmed objective response only.
NR = not reached.
Meric-Bernstam F, et al. *J Clin Oncol*. 2023;42(1):47-58. Slide courtesy of Meric-Bernstam F.

HER2 Antibody-Drug Conjugates

ADC	Abbr.	Ab	Payload	DAR	Linker
Trastuzumab emtansine	T-DM1	Trastuzumab	DM1	3.5	noncleavable
Trastuzumab deruxtecan	T-DXd	Trastuzumab	DXd	8	cleavable
Disitamab vedotin	DV	Hertuzumab	MMAE	4	cleavable

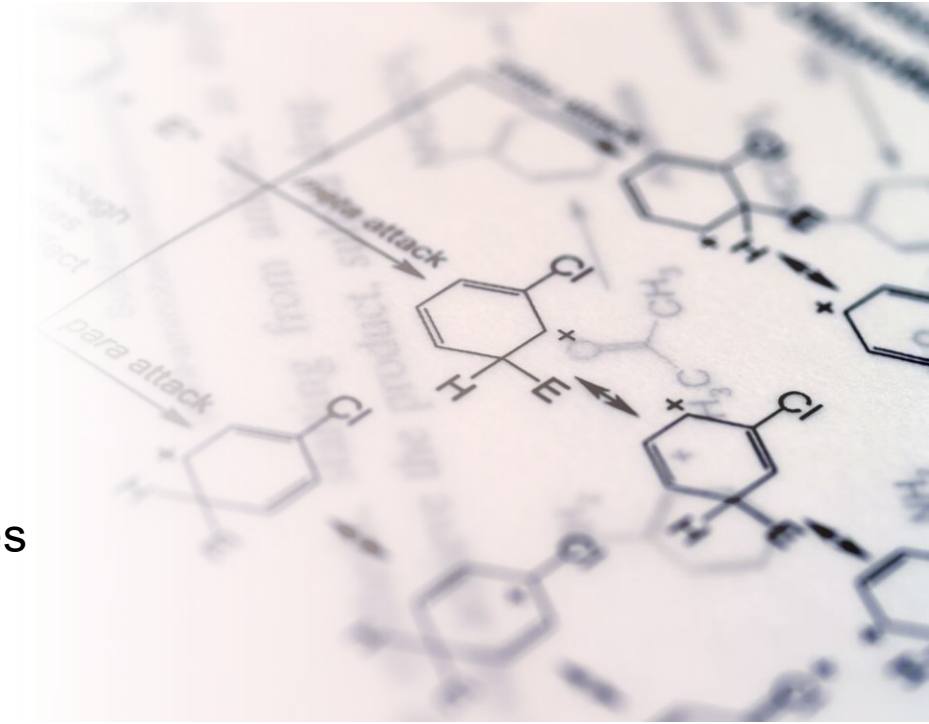
Other HER2 ADCs:
ARX788 (AS269), ALT-P7 (MMAE), SYD985 (Duba), MTG002 (MMAE), A166 (Duo-5), ZW49 (ZD02044), LCB14/IKSO14, etc.

Other payloads:
ORM-5029 (SMol006:GSPT1 degrader), XMT-2056 (STING agonist)

MMAE = monomethyl auristatin E.
Adapted from Colombo R, Rich JR. *Cancer Cell*. 2022;40(11):1255-1263. Slide courtesy of Meric-Bernstam F.

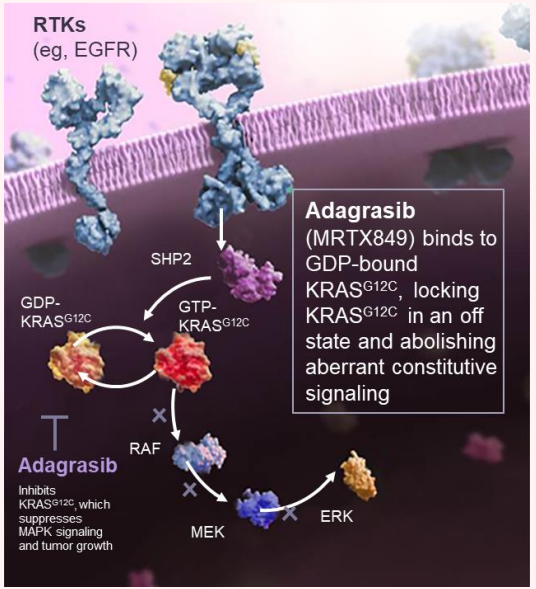
Agenda

- Emergence of tumor-agnostic therapy
- 3 examples
  - Larotrectinib
  - Dabarafenib and tremetinib
  - Trastuzumab deruxtecan (T-DXd)
- Emerging new tumor-agnostic therapies



Adagrasib (MRTX849) Is a Differentiated KRASG12C Inhibitor

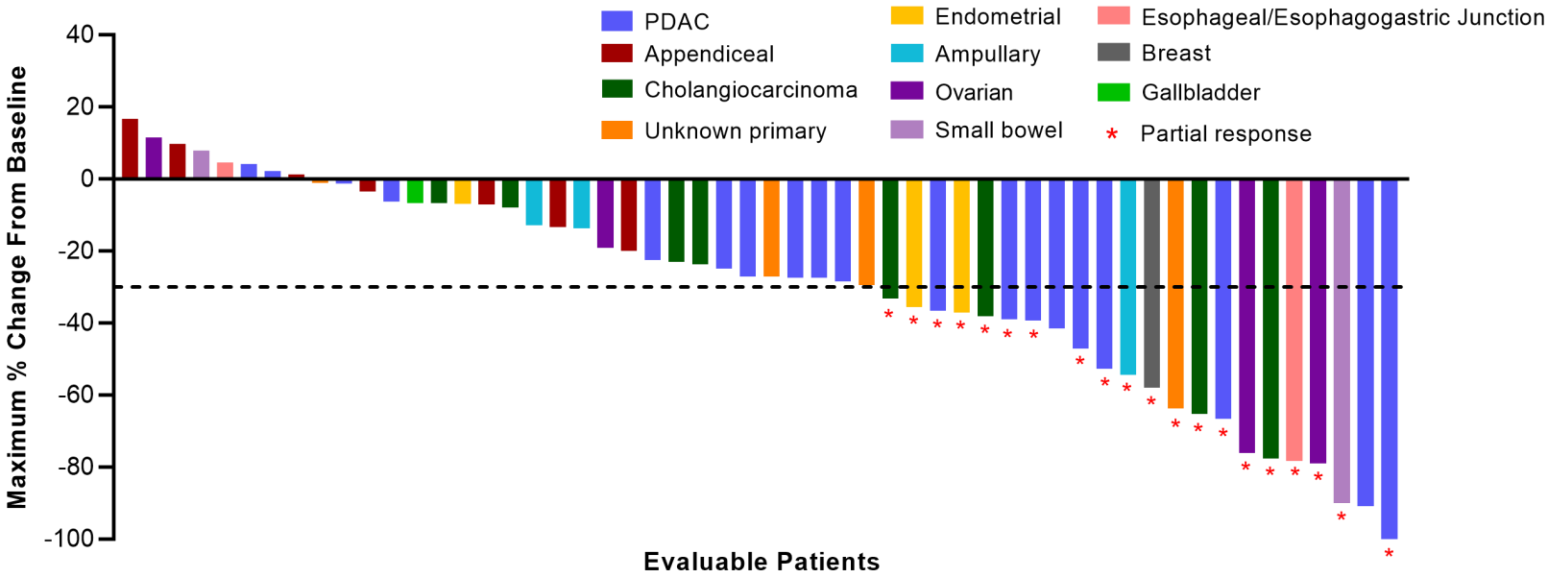
- KRAS^{G12C} mutations act as oncogenic drivers in a range of solid tumors
  - NSCLC (~14%)
  - CRC (3-4%)
  - Appendiceal (3-4%)
  - Ovarian (0.4%)
  - PDAC (1-3%)
  - Small bowel (1-3%)
  - Biliary tract (1%)
  - Endometrial (1.5%)
- Adagrasib, a covalent inhibitor of KRAS^{G12C}, was selected for favorable properties, including a long half-life (23 hours), dose-dependent PK and CNS penetration
- Adagrasib has been granted accelerated approval by the FDA and is under review by the EMA for the treatment of KRAS^{G12C}-mutated NSCLC
- Adagrasib has been granted breakthrough therapy designation, in combination with cetuximab, for the treatment of patients with KRAS^{G12C}-mutated CRC



PK = pharmacokinetics; CNS = central nervous system; EMA = European Medicines Agency.

Pant S, et al. *J Clin Oncol*. 2023;41(36 Suppl):425082. Slide courtesy of Pant S.

Adagrasib in Patients with Solid Tumors[a]: Best Tumor Change from Baseline

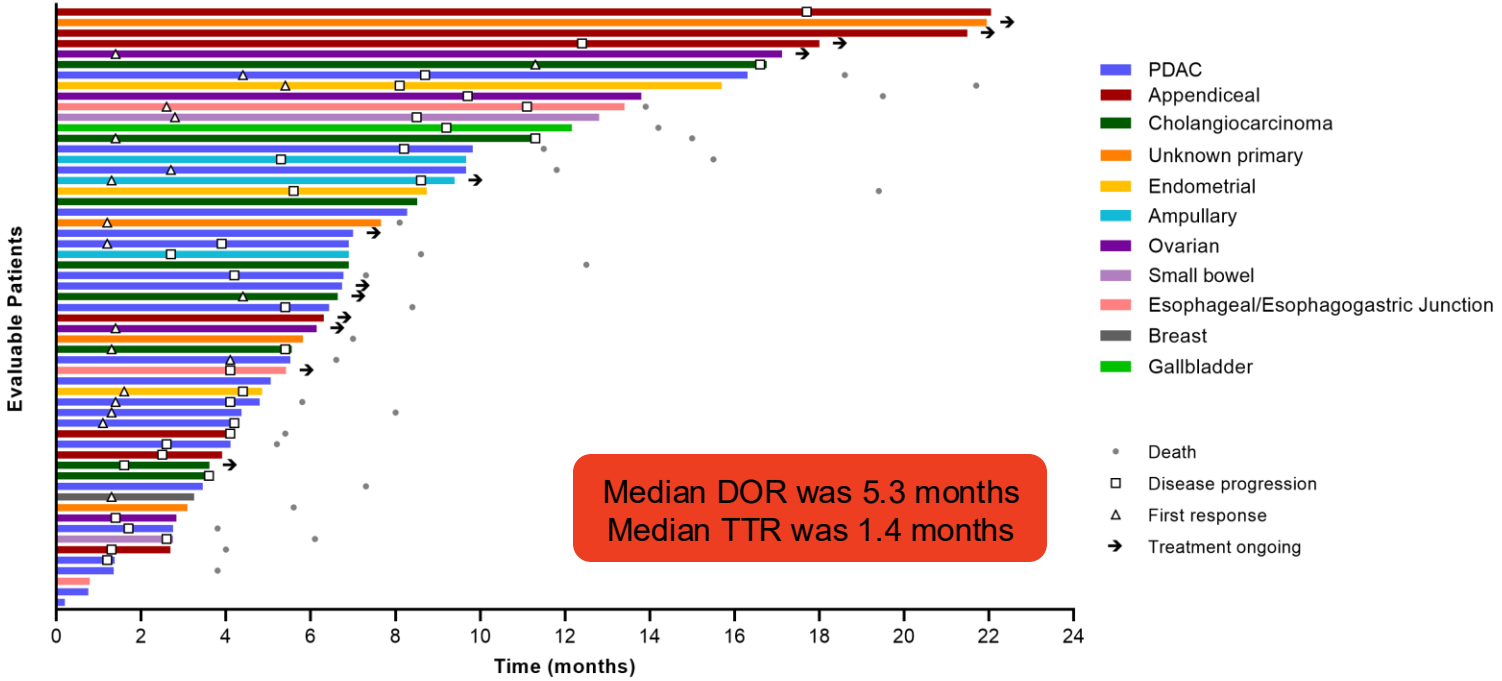


- Confirmed objective responses were observed in 20/57 patients (35.1%)
- Disease control was observed in 49/57 patients (86.0%)

[a]Excluding non-small cell lung cancer and colorectal cancer. All results are based on BICR; data as of October 1, 2022 (median follow-up: 16.8 months).
PDAC = pancreatic ductal adenocarcinoma; BICR = blinded independent central review.
Pant S, et al. *J Clin Oncol*. 2023;41(36 Suppl):425082. Slide courtesy of Pant S.

Great Debates Solid Tumors

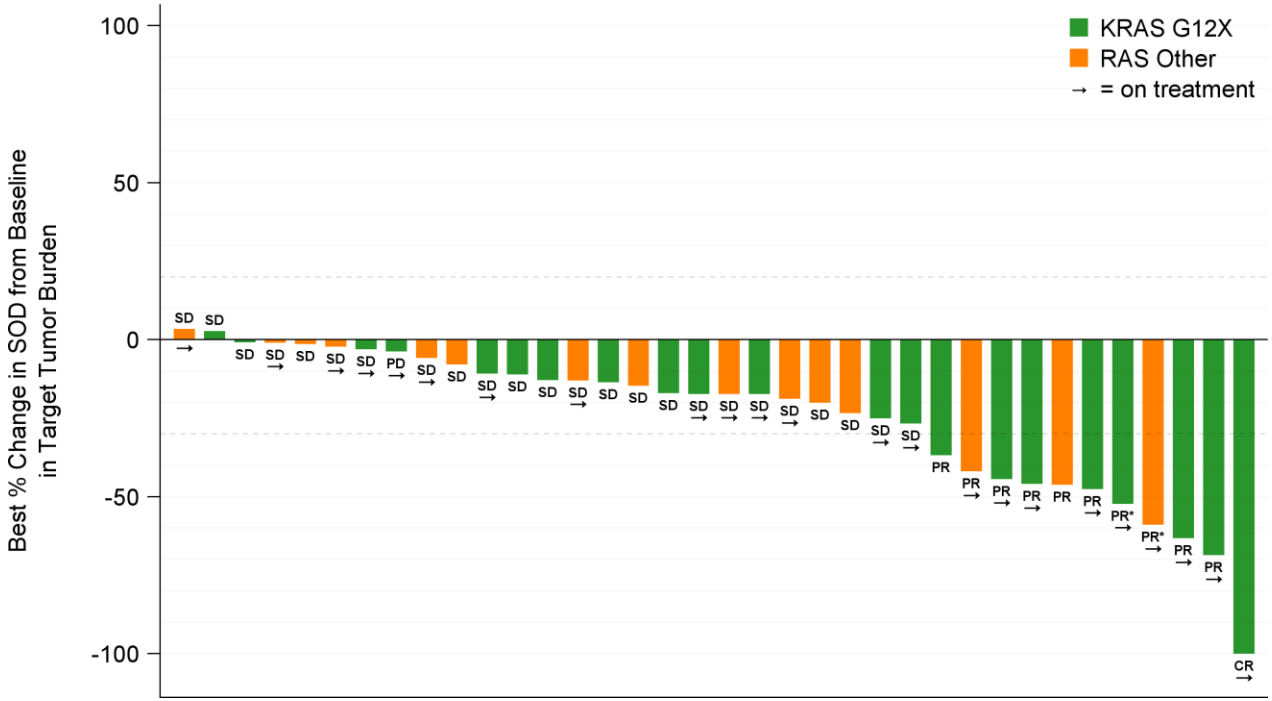
Adagrasib in Patients with Solid Tumors[a]: Duration of Treatment



[a]Excluding non-small cell lung cancer and colorectal cancer. All results are based on BICR; data as of October 1, 2022 (median follow-up: 16.8 months).
TTR = time to response.
Pant S, et al. *J Clin Oncol*. 2023;41(36 Suppl):425082. Slide courtesy of Pant S.

Great Debates Solid Tumors

Encouraging Objective Response Rates in 2L Patients with PDAC Treated with RMC-6236 at 300 mg Daily

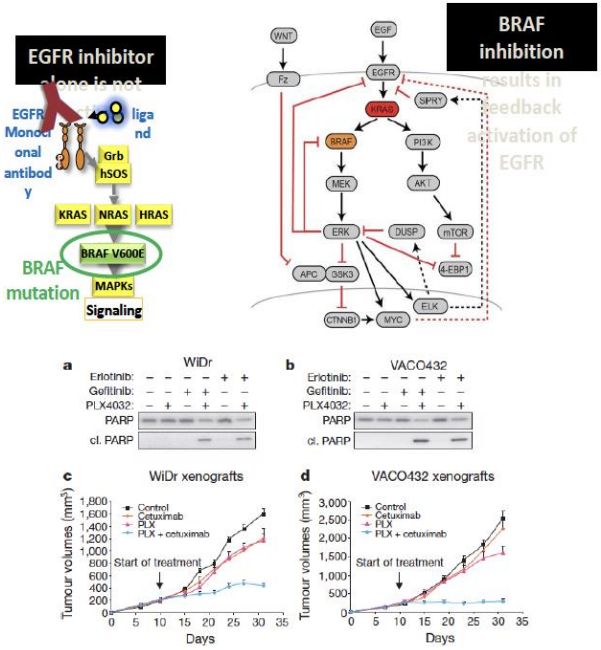


	ORR
KRAS G12X	**36%** (8/22)
RAS Mutant[(1)]	**27%** (10/37)

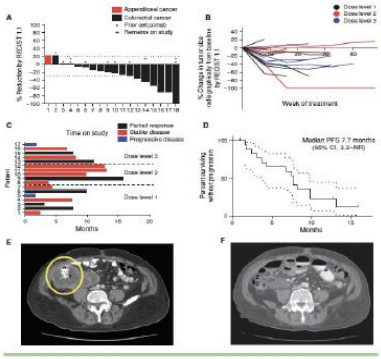
ENA 2024 data set (data cutoff: Jul 23, 2024).
(1) RAS Mutant defined as patients with G12X, G13X or Q61X PDAC.
KRAS G12X mutation includes any KRAS mutation where glycine (G) at position 12 is substituted by another amino acid. RAS Other includes mutations in KRAS G13X, KRAS Q61X, or mutations in HRAS or NRAS at codons G12X, G13X, or Q61X. Among patients with a response (confirmed or unconfirmed), 46% of first response occurred within 2 months of RMC-6236 treatment. 2L in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose. ORR analyses included all patients who received first dose of RMC-6236 at least 14 weeks prior to data cutoff date (to allow 2 potential scans). Unconfirmed PRs (PR*) with treatment discontinued (will never confirm) were not considered responders but remain in the denominator; ORR (by RECIST v1.1) includes confirmed CRs/PRs and unconfirmed CRs/PRs who were still on treatment and may yet be confirmed. One patient included in the denominator of the ORR analyses is not displayed on waterfall due to lack of post-baseline target lesion assessment (patient withdrew consent).
PR* = unconfirmed PR; SOD = sum of diameters.
Wolpin B, et al. Presented at: EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics; October 23-25, 2024; Barcelona, Spain. Abstract 514LBA (PB-514).

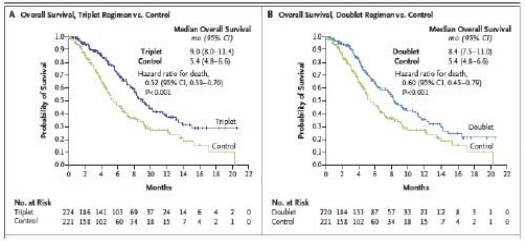
Lessons from BRAF in CRC

BRAF Inhibition Leads to EGFR Feedback

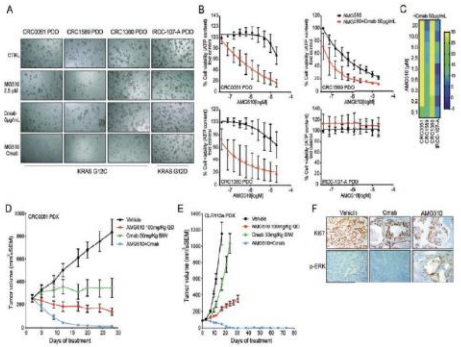


BRAF Inhibition + Inhibition of EGFR Feedback Provides Clinical Benefit (ORR,PFS,OS)





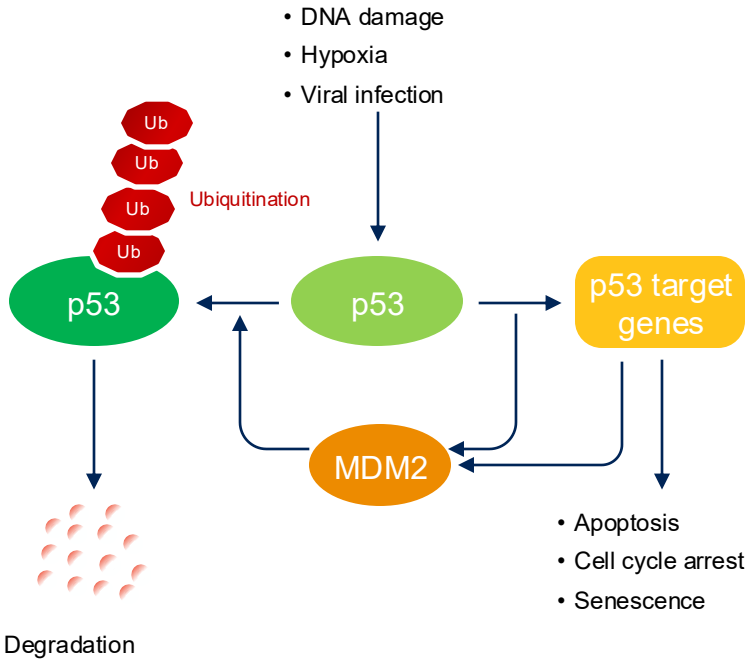
EGFR blockade reverts resistance to KRAS ^{G12C} inhibition in colorectal cancer



Prahallad A, et al. Nature. 2012;483(7387):100-103. Hong DS, et al. *Cancer Discov*. 2016;6(12):1352-1365. Kopetz S, et al. *N Engl J Med*. 2019;381(17):1632-1643. Amodio V, et al. *Cancer Discov*. 2020;10(8):1129-1139.

Great Debates Solid Tumors

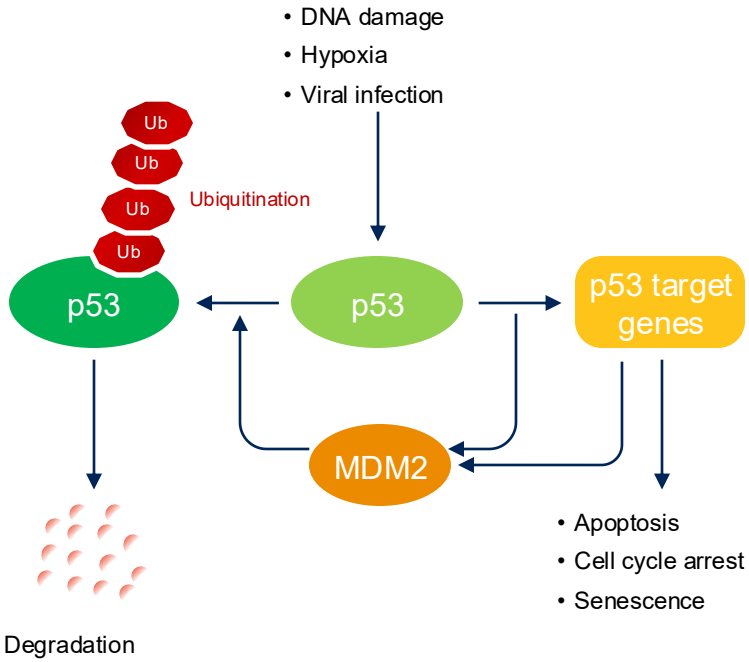
Role of p53 and Ways to Reactivate p53 in Solid Tumors



- The p53 protein binds to DNA and has key roles in cell cycle arrest, DNA repair, and apoptosis
  - Activated following cellular stress and DNA damage
  - Supports DNA repair before cellular replication
  - Induces apoptosis
- Protein levels are tightly controlled by MDM2
- *TP53* mutation resulting in p53 inactivation is a key step in oncogenesis

Dumbrava EE, et al. *J Clin Oncol*. 2022;40(16 Suppl):3003. Chillemi G, et al. *Cold Spring Harb Perspect Med*. 2017;7(4):a028308. Kastenhuber ER, et al. *Cell*. 2017;170(6):1062-1078. Levine AJ. *Nat Rev Cancer*. 2020;20(8):471-480. Levine AJ. *J Mol Cell Biol*. 2019;11(7):524-530. Slide courtesy of Dumbrava E.

Role of p53 and Ways to Reactivate p53 in Solid Tumors



I. **Targeting specific p53 mutations→ PC14586**

II. **II. Targeting MDM2→ MDM2 antagonists**

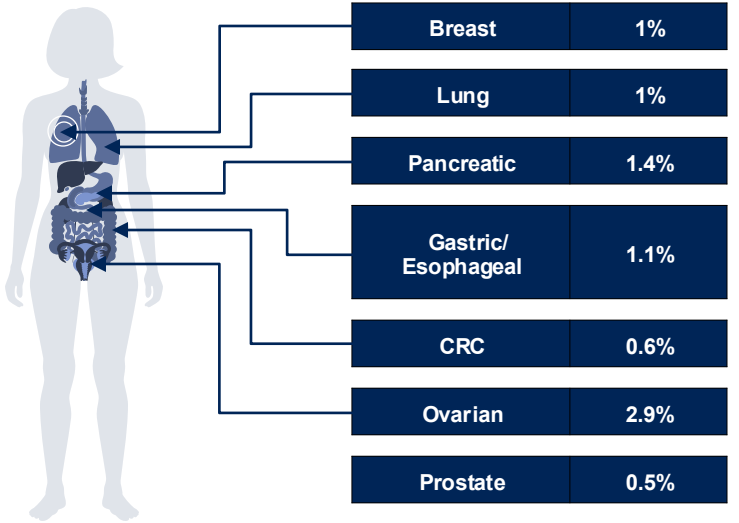
Dumbrava EE, et al. *J Clin Oncol*. 2022;40(16 Suppl):3003. Slide courtesy of Dumbrava E.

TP53 Y220C Hotspot Mutation Is Detected across Solid Tumor Types

- *TP53* mutations are the most common genomic events across all human cancers
- Most *TP53* mutations occur in the central DNA-binding domain, and ten of them are referred to as “hot-spot” mutations, accounting for ~30% of the *TP53* mutations observed in human cancer
- p53 Y220C is a key hot-spot *TP53* missense mutation that destabilizes p53
- p53 Y220C is present in ~1% of all solid tumors

Frequency of *TP53 Y220C* across Common Solid Tumors

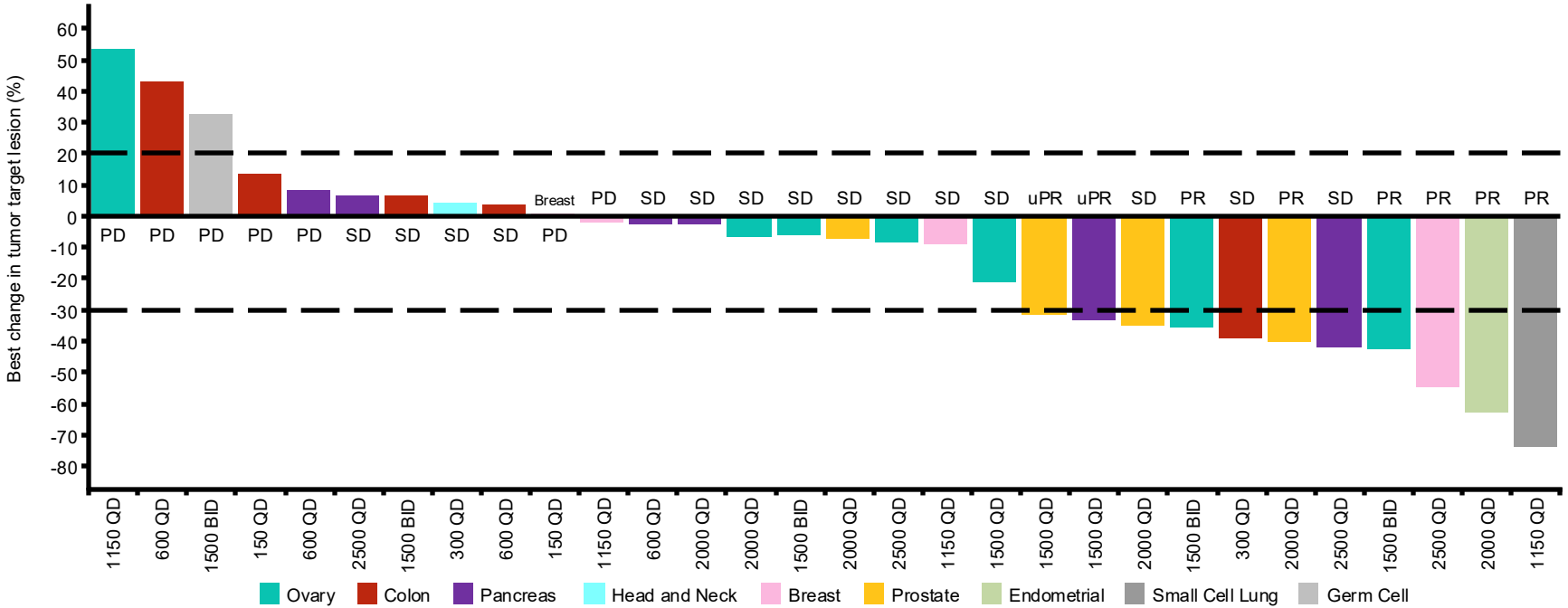
Tissue and heme assay test results
collected between 1/1/12 and 12/31/2020



The prevalence of TP53 Y220C across different diseases was analyzed by using a web-based software platform to query a pan-solid tumor cohort of ~367,651 US-based, consented-for-research patients in the platform’s database who received commercial tissue or heme assays between 1/1/12 and 12/31/2020.

Dumbrava EE, et al. *J Clin Oncol*. 2022;40(16 Suppl):3003. Baugh EH, et al. *Cell Death Differ*. 2018;25,154-160. Roszkowska KA, et al. *Int J Mol Sci*. 2020;21:1334. Bouaoun L, et al. *Hum Mutat*. 2016;37:865-876. Westphalen CB, et al. *NPJ Precis Oncol*. 2021;20;5(1):69. Slide courtesy of Dumbrava E.

Target Lesion Reduction across Tumor Types



Data cutoff May 10, 2022.
Includes patients with measurable disease and one post-baseline assessment. All doses are in mg.
uPR = unconfirmed PR pending confirmation.
Dumbrava EE, et al. *J Clin Oncol*. 2022;40(16 Suppl):3003. Slide courtesy of Dumbrava E.

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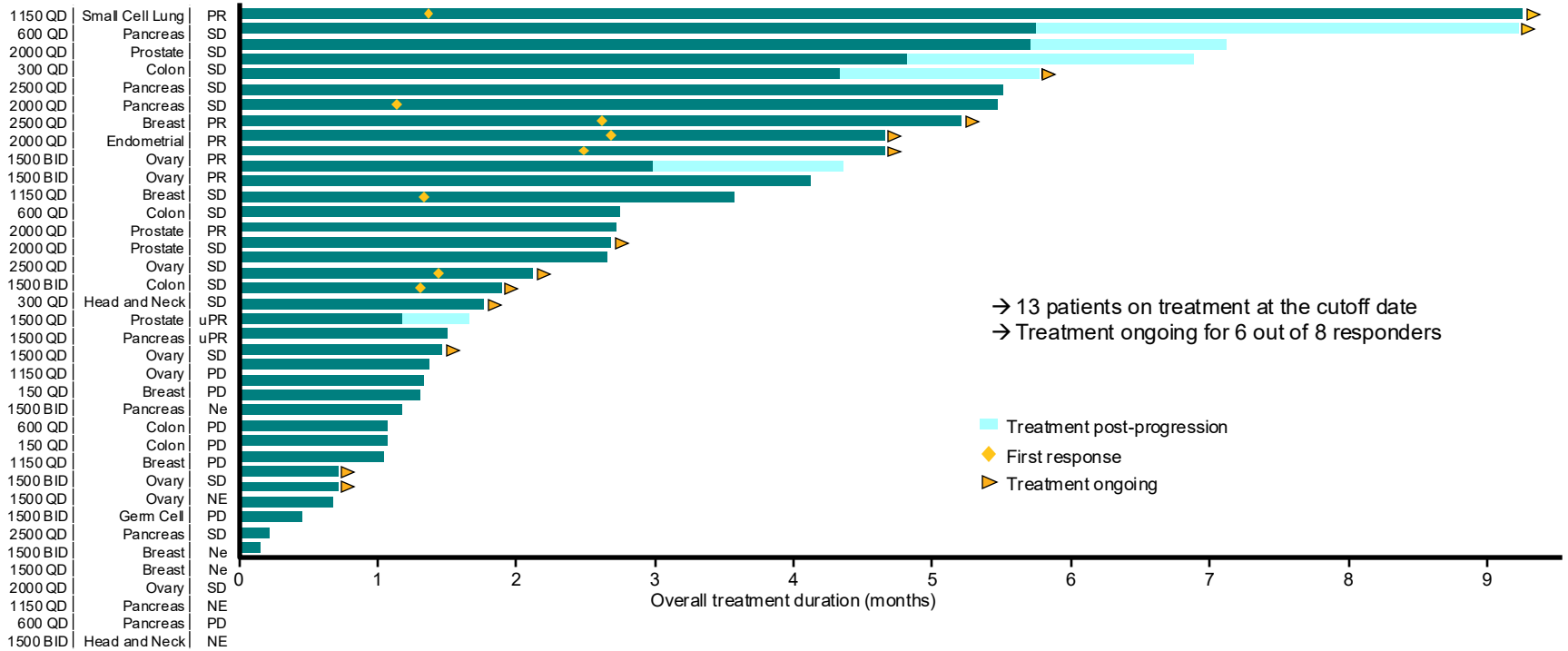
Duration of PC14586 Therapy



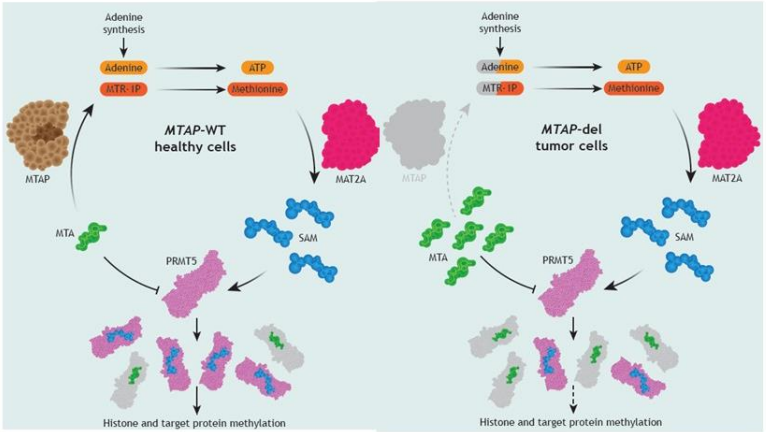
Data cutoff May 10, 2022.
Includes all patients with measurable disease at baseline (n=36). All doses are in mg.
Ne = not eligible for response assessment.
Dumbrava EE, et al. *J Clin Oncol*. 2022;40(16 Suppl):3003. Slide courtesy of Dumbrava E.

Great Debates Solid Tumors

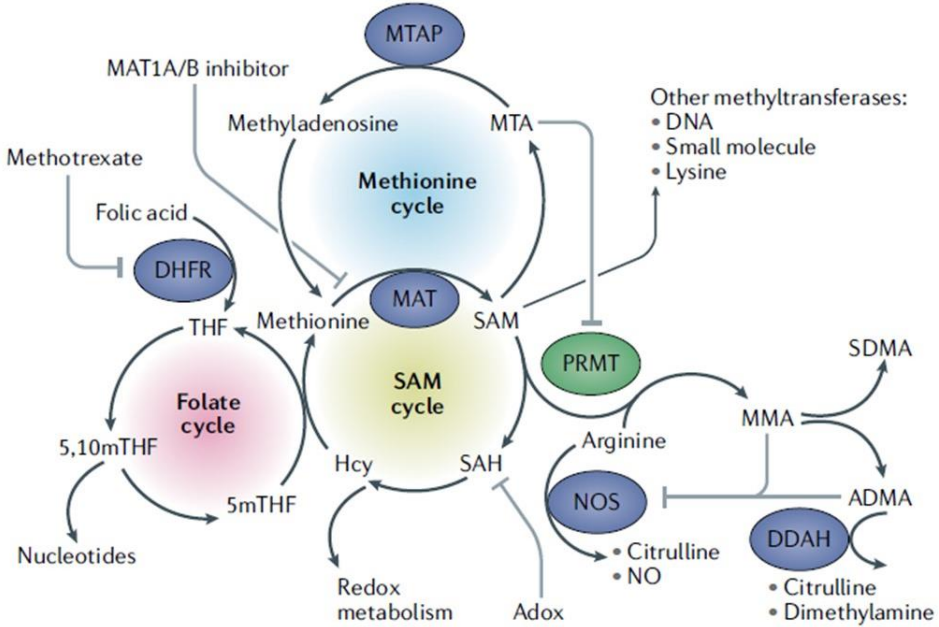
Background of MTAP

MTAP: the only enzyme in mammalian cells known to catalyze MTA, plays a major role in the salvage of both adenine and methionine

MTAP is located in 9p21, a region with frequent homozygous deletions



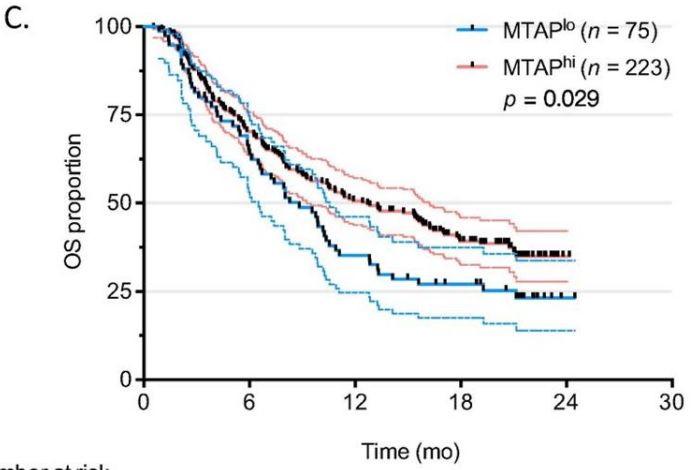
MTA: MethylThioAdenosine
MTAP: MethylThioAdenosine Phosphorylase
SAM: S-Adenosyl Methyonine

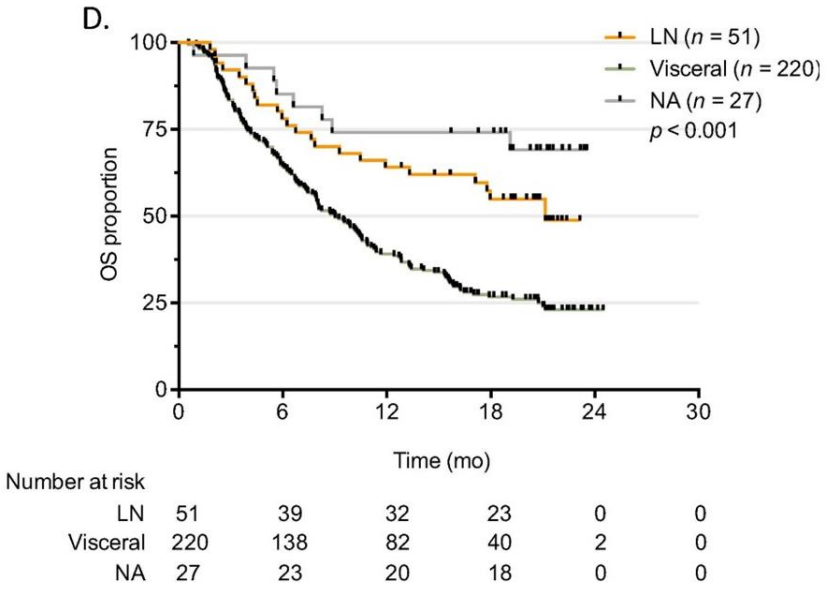


Rodon J. Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois. Slide courtesy Rodon J.

Prognostic Factor of 9p21/MTAP Loss

MTAP loss correlates with worse OS and higher risk of metastasis in bladder cancer

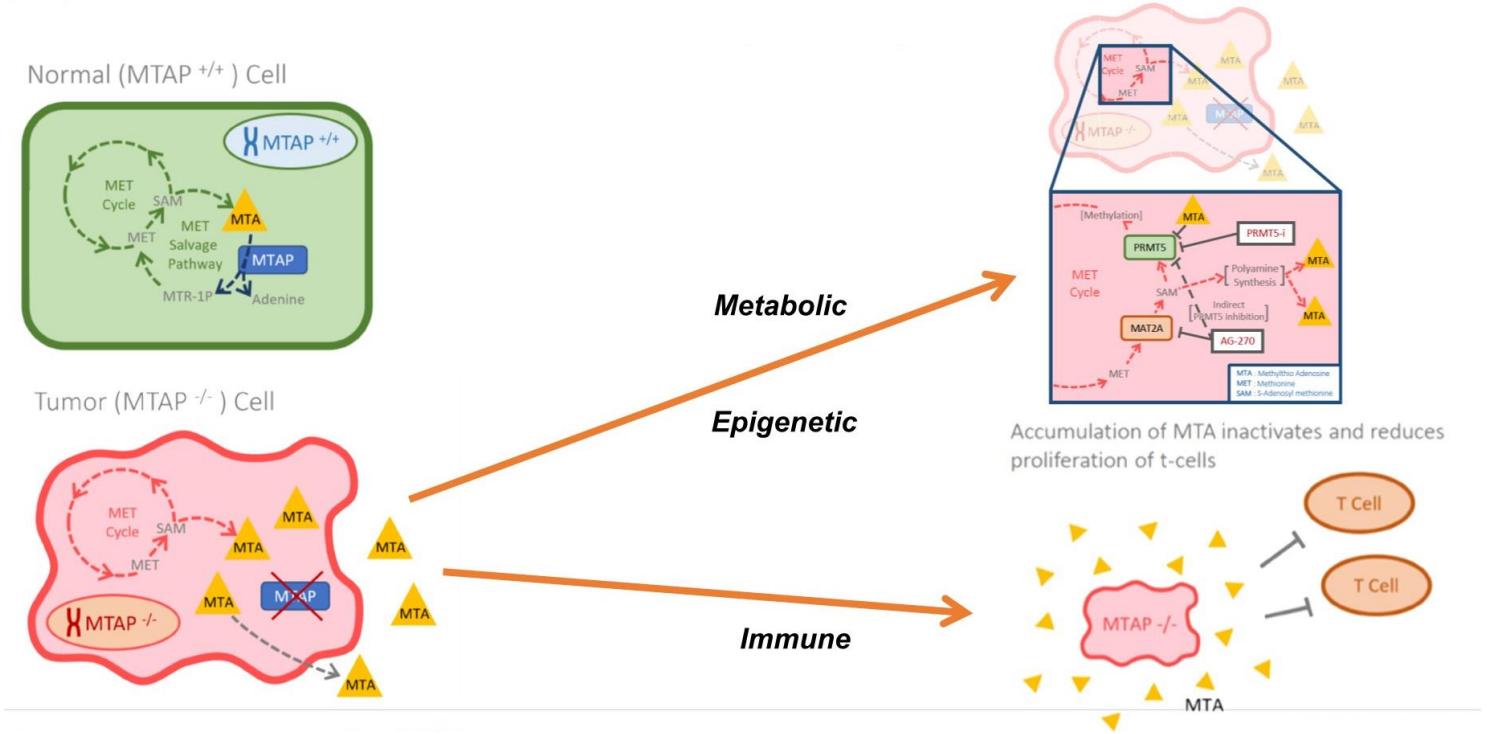




Similar results seen in NSCLC, Mesothelioma and Pancreas

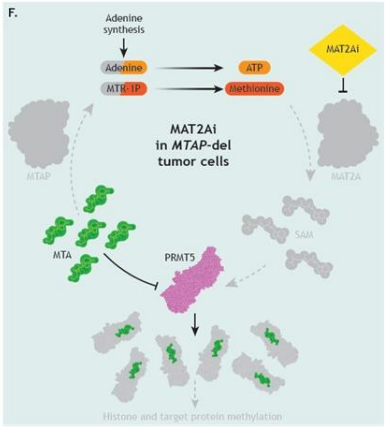
Rodon J. Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois. Alhalabi O, et al. *Eur Urol Oncol*. 2023;6(6):611-620. Slide courtesy Rodon J.

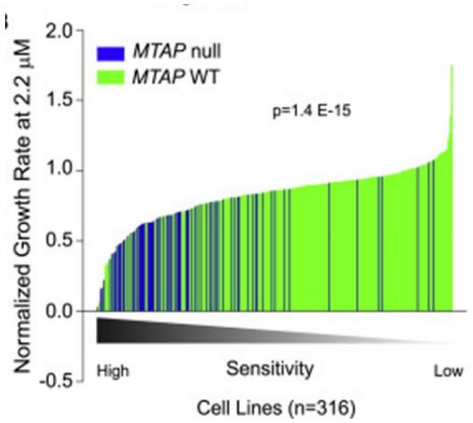
MTAP Loss Disrupts Metabolic, Epigenetic, and Immune-Related Pathways

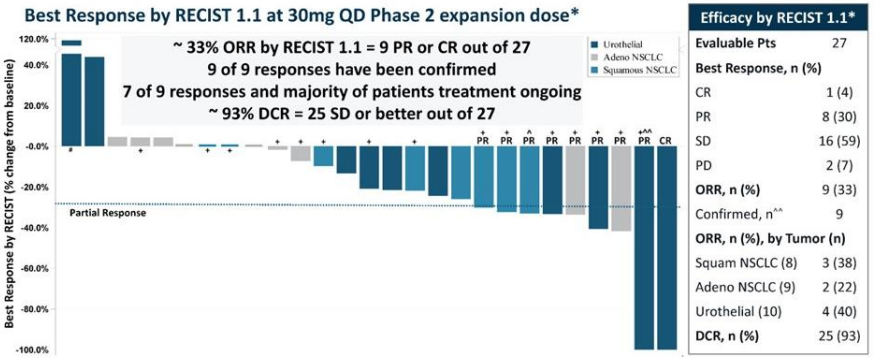


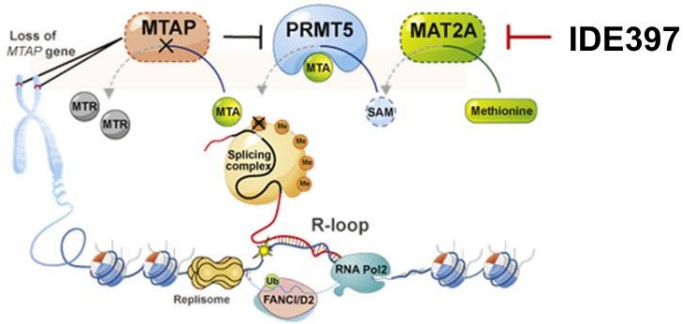
Rodon J. Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois. Slide courtesy Rodon J.

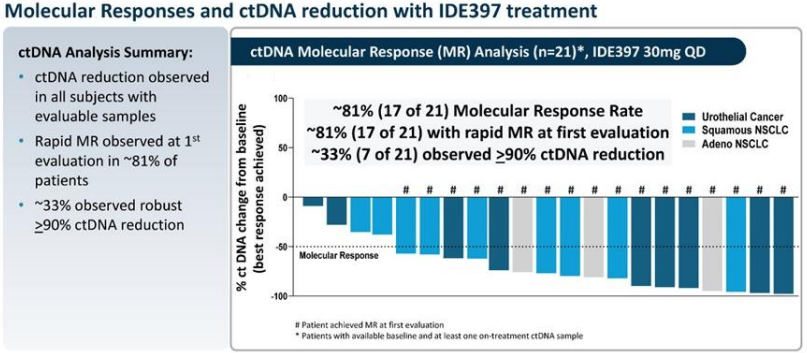
First-in-Human Trial of IDE397 (MAT2A Inhibitor)







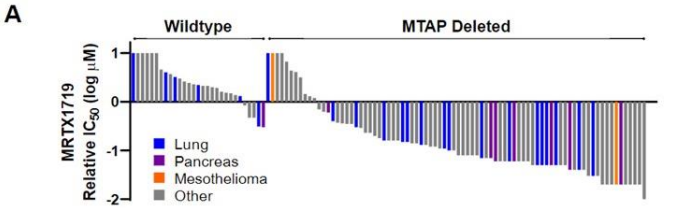


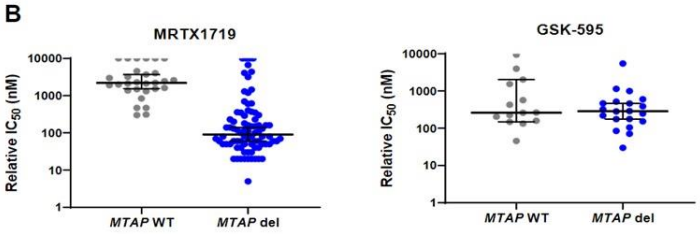


DCR = disease control rate; ctDNA = circulating tumor DNA.

Rodon J. Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois. Adapted from Kalev P, et al. *Cancer Cell*. 2021;39(2):209-224.e11. Herzberg B, et al. Presented at: ENA Symposium on Molecular Targets and Cancer Therapeutics; October 23-25, 2024; Barcelona, Spain. Abstract 501LBA. Slide courtesy Rodon J.

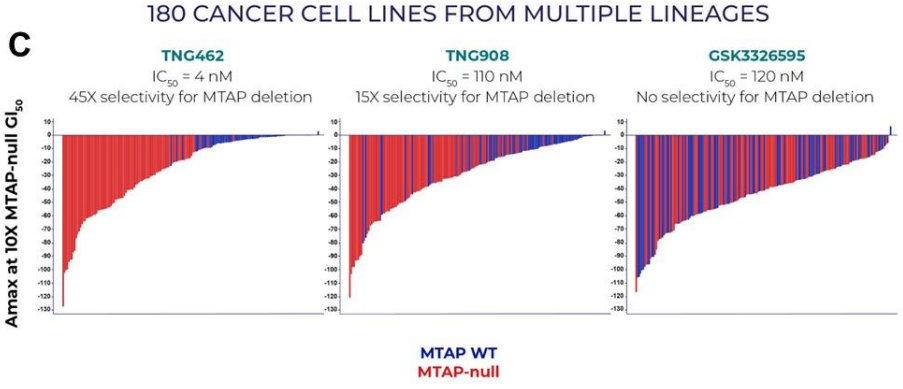
MTA-Cooperative PRMT5 Inhibitors Show Improved Selectivity to MTAP Loss Tumors

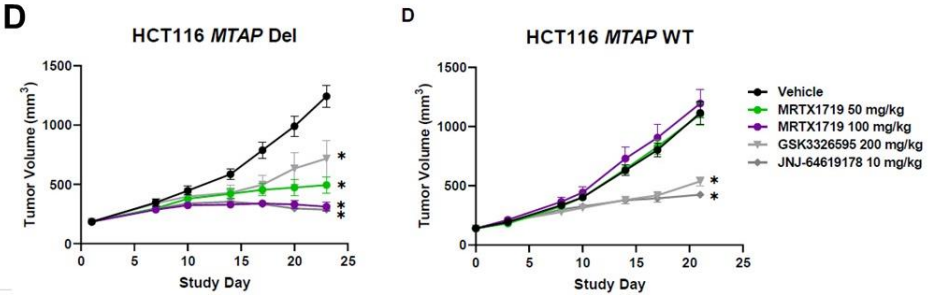




A. and **B.** MRTX1719 and GSK3326595 (B) in vitro activity across a panel of *MTAP* WT and *MTAP* del cell line models (5-day viability assay, Crown Biosciences) along with table listing median IC_{50}s and *MTAP* WT over *MTAP* del fold selectivity (B)

	Median IC_{50} (nM)	
	MRTX1719	GSK595
MTAP WT	2200	286
MTAP del	90	262
Fold Selectivity	24	1





WT = wild-type.

Rodon J. Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois. Slide courtesy Rodon J.

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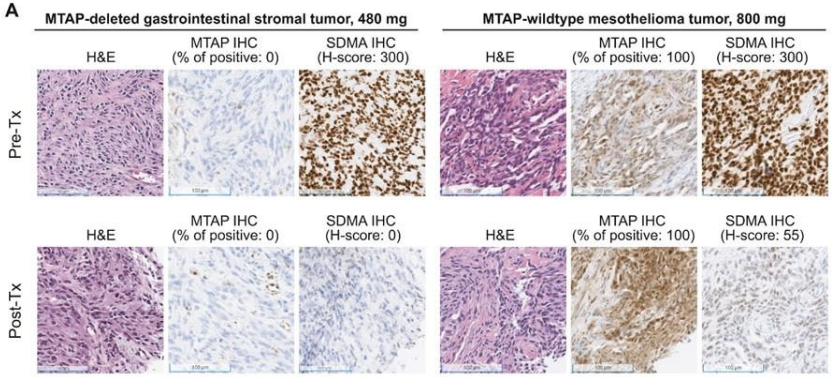
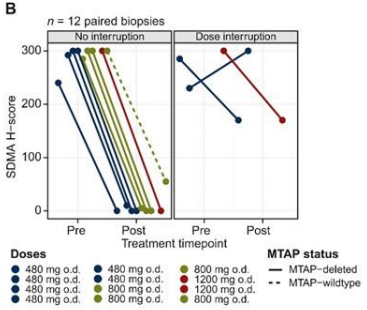
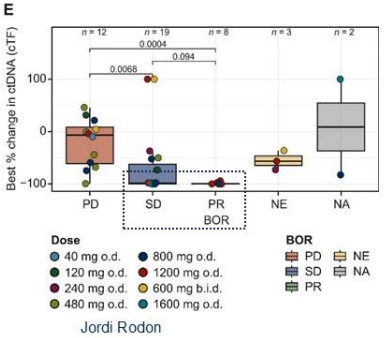
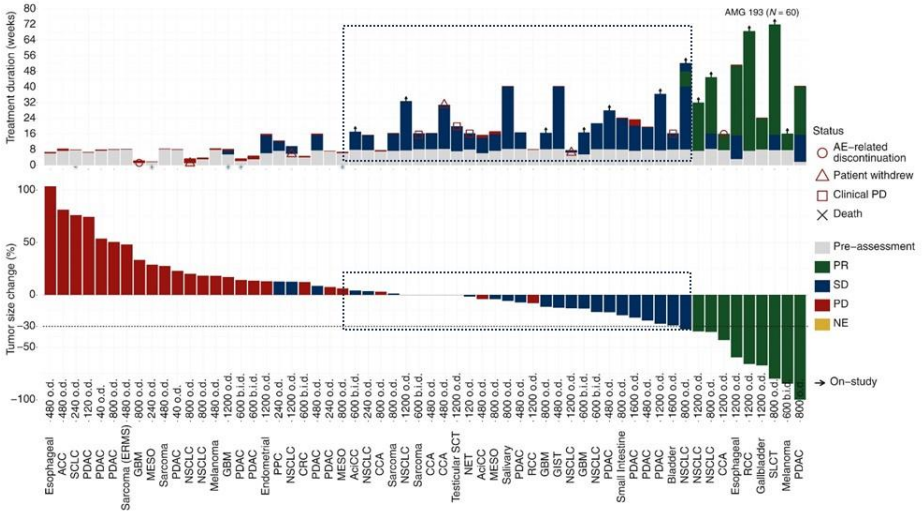
First-in-Human Trial of AMG193 (MTA-Cooperative PRMT5 Inhibitor)







Jordi Rodon



Partial Responses in:

- Bladder
- NSCLC
- Pancreas
- Esophageal
- Cholangio
- Gallbladder
- RCC
- Melanoma
- SLCT

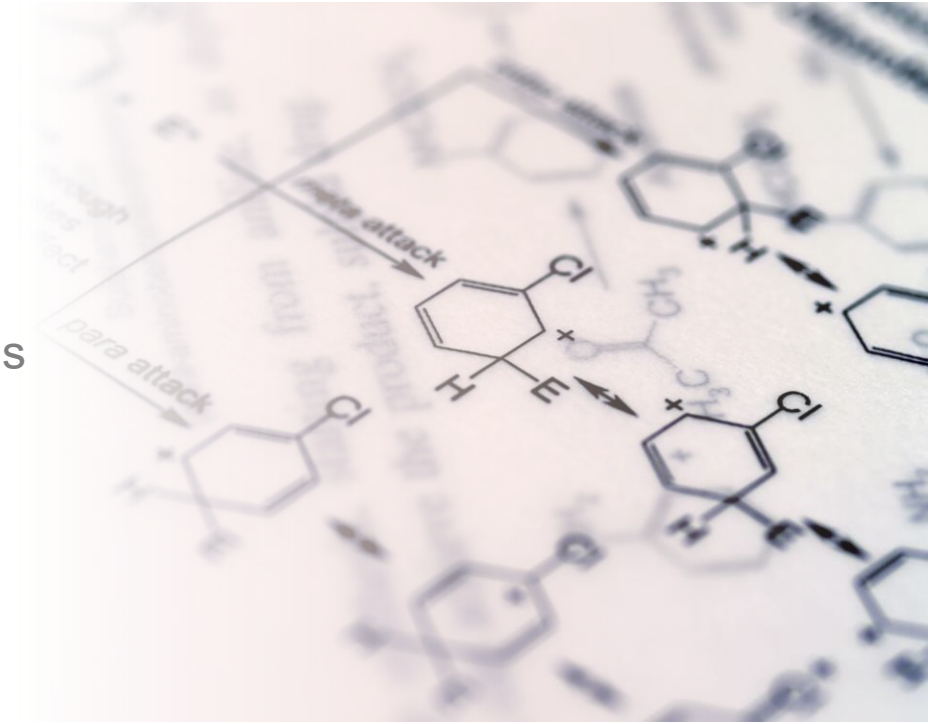
H&E = hematoxylin, eosin; SDMA = symmetric dimethylarginine; AE = adverse event; SLCT = Sertoli-Leydig cell tumor.

Rodon J. Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois. Rodon J, et al. *Ann Oncol*. 2024;35(12):1138-1147. Slide courtesy Rodon J.

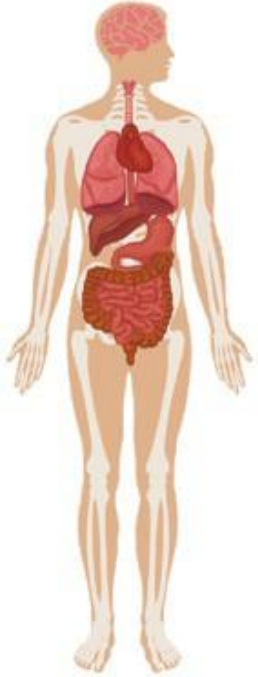
Great Debates Solid Tumors

Agenda

- Emergence of tumor-agnostic therapy
- 3 examples
- Emerging new tumor-agnostic therapies
- Challenges

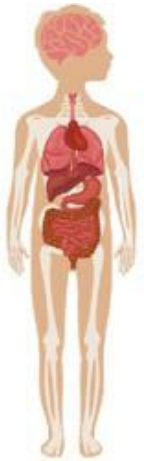


Adult



- Brain cancers (0.4-3.1%)
- Salivary (MASC; 90-100%)
- Secretory breast cancer (92%)
- Pancreatic cancer
- Cholangiocarcinoma (3.6%)
- Thyroid cancer (1.5-14.5%)
- Lung cancer (0.23.3%) ←
- GIST (3.2%)
- Colon cancer (1.5%) ←
- Melanoma (0.3%)
- Sarcomas (1%)*

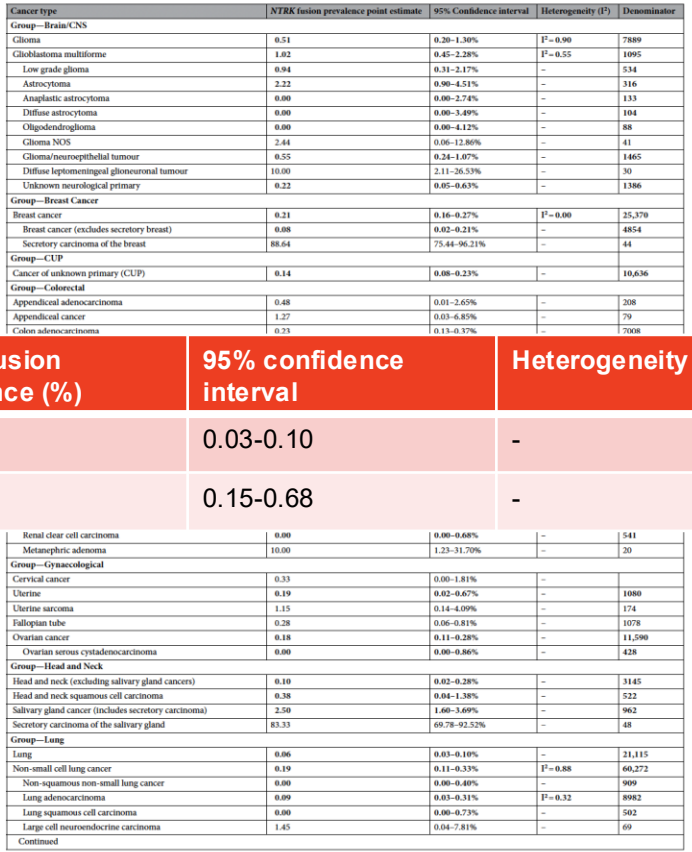
Pediatric



- Spitzoid neoplasms (16.4%)
- Gliomas (7.1%)
- Thyroid (9.4–25.9%)
- Infantile fibrosarcoma (91–100%)
- Congenital nephroma (83%)
- Secretory breast cancer (92%)*
- Sarcomas (1%)*

***Frequency in adult vs pediatric patients not specified.**
MASC = mammary analogue secretory carcinoma.
MSL slide deck. November 2018.

You're Never as Big as You Think!



Cancer type	*NTRK* fusion prevalence point estimate	95% Confidence interval	Heterogeneity (I^2)	Denominator
Group—Brain/CNS				
Glioma	0.51	0.20–1.30%	$I^2 = 0.90$	7889
Glioblastoma multiforme	1.02	0.45–2.28%	$I^2 = 0.55$	1095
Low grade glioma	0.94	0.31–2.17%	–	534
Astrocytoma	2.22	0.90–4.51%	–	316
Anaplastic astrocytoma	0.00	0.00–2.74%	–	133
Diffuse astrocytoma	0.00	0.00–3.49%	–	104
Oligodendroglioma	0.00	0.00–4.12%	–	88
Glioma NOS	2.44	0.06–12.86%	–	41
Glioma/neuroepithelial tumour	0.55	0.24–1.07%	–	1465
Diffuse leptomeningeal glioneuronal tumour	10.00	2.11–26.53%	–	30
Unknown neurological primary	0.22	0.05–0.63%	–	1386
Group—Breast Cancer				
Breast cancer	0.21	0.16–0.27%	$I^2 = 0.00$	25,370
Breast cancer (excludes secretory breast)	0.08	0.02–0.21%	–	4854
Secretory carcinoma of the breast	88.64	75.44–96.21%	–	44
Group—CUP				
Cancer of unknown primary (CUP)	0.14	0.08–0.23%	–	10,636
Group—Colorectal				
Appendiceal adenocarcinoma	0.48	0.01–2.65%	–	208
Appendiceal cancer	1.27	0.03–6.85%	–	79
Colon adenocarcinoma	0.23	0.13–0.37%	–	7008
Renal clear cell carcinoma	0.00	0.00–0.68%	–	541
Metanephric adenoma	10.00	1.23–31.70%	–	20
Group—Gynaecological				
Cervical cancer	0.33	0.00–1.81%	–	
Uterine	0.19	0.02–0.67%	–	1080
Uterine sarcoma	1.15	0.14–4.09%	–	174
Fallopian tube	0.28	0.06–0.81%	–	1078
Ovarian cancer	0.18	0.11–0.28%	–	11,590
Ovarian serous cystadenocarcinoma	0.00	0.00–0.86%	–	428
Group—Head and Neck				
Head and neck (excluding salivary gland cancers)	0.10	0.02–0.28%	–	3145
Head and neck squamous cell carcinoma	0.38	0.04–1.38%	–	522
Salivary gland cancer (includes secretory carcinoma)	2.50	1.60–3.69%	–	962
Secretory carcinoma of the salivary gland	83.33	69.78–92.52%	–	48
Group—Lung				
Lung	0.06	0.03–0.10%	–	21,115
Non-small cell lung cancer	0.19	0.11–0.33%	$I^2 = 0.88$	60,272
Non-squamous non-small lung cancer	0.00	0.00–0.40%	–	909
Lung adenocarcinoma	0.09	0.03–0.31%	$I^2 = 0.32$	8982
Lung squamous cell carcinoma	0.00	0.00–0.73%	–	502
Large cell neuroendocrine carcinoma	1.45	0.04–7.81%	–	69
Continued				

Cancer Type	NTRK Fusion Prevalence (%)	95% confidence interval	Heterogeneity	Denominator
Lung	0.06	0.03-0.10	-	21115
CRC	0.35	0.15-0.68	-	2306

O'Haire S, et al. *Sci Rep*. 2023;13(1):4116.

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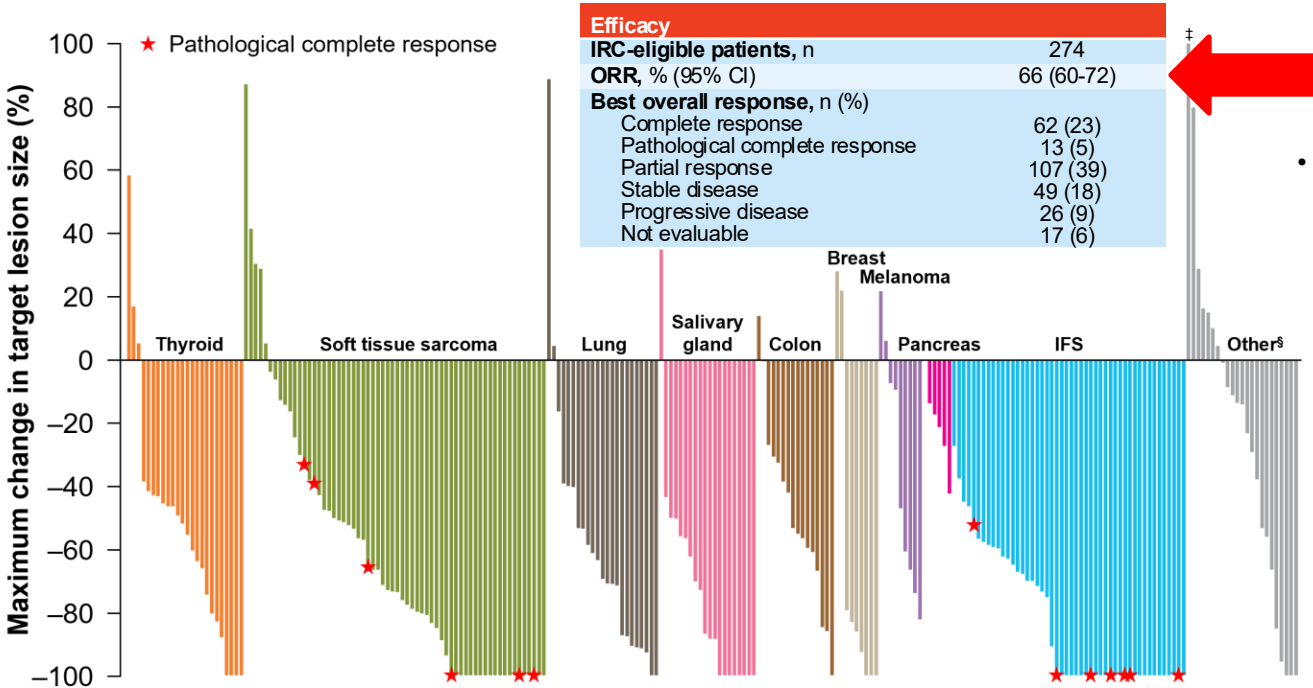
You're Never as Big as You Think!

Efficacy

Maximum change in target lesion size in patients with TRK fusion cancer (n=240)†



Efficacy	
IRC-eligible patients, n	274
ORR, % (95% CI)	66 (60-72)
Best overall response, n (%)	
Complete response	62 (23)
Pathological complete response	13 (5)
Partial response	107 (39)
Stable disease	49 (18)
Progressive disease	26 (9)
Not evaluable	17 (6)

Larotrectinib was efficacious across most tumor types

- The original 55 patients from the July 2018 primary data cutoff were included for long-term follow-up
  - At data cut-off, ORR per IRC was 75% (95% CI 61-85).
  - Eight patients had an improved best overall response from partial response to complete response (or pathological complete response), with a total complete response rate of 27%
  - Of the original 55 patients, 10 are still on treatment
  - Twelve patients were progression-free when they discontinued treatment

†Thirty-four patients had no measurable lesions or had missing data as assessed by IRC. ‡Patient had a maximum charge in target lesion size of +277%. §Other includes appendix, bone sarcoma, cancer of unknown primary, cervix, cholangiocarcinoma, congenital mesoblastic nephroma, duodenal, external auditory canal, gastric, gastrointestinal stromal tumor, hepatic, esophageal, prostate, rectal, thymus, urothelial, and uterus.

Drilon A, et al. Presented at: ESMO 2023 Annual Meeting; October 20-24, 2023; Madrid, Spain. Abstract 3406.

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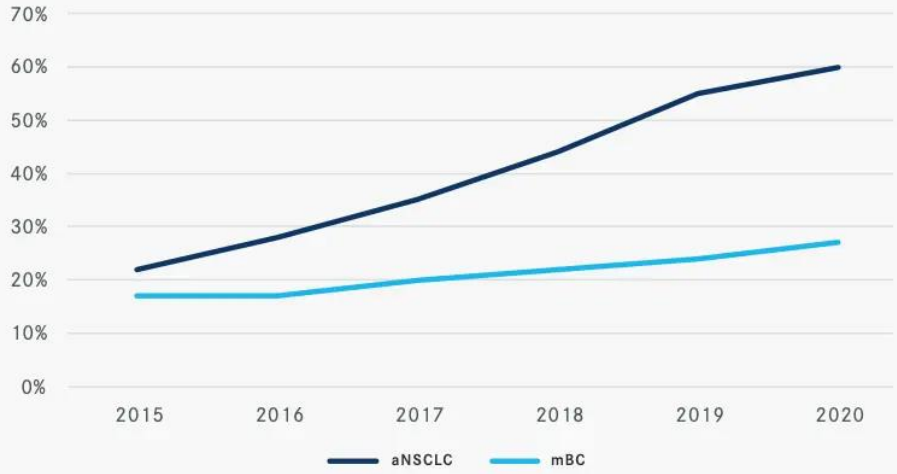
They Don’t Care as Much as You Do!

NGS for patients with NSCLC (n=29,572) and metastatic breast cancer (n=12,175)

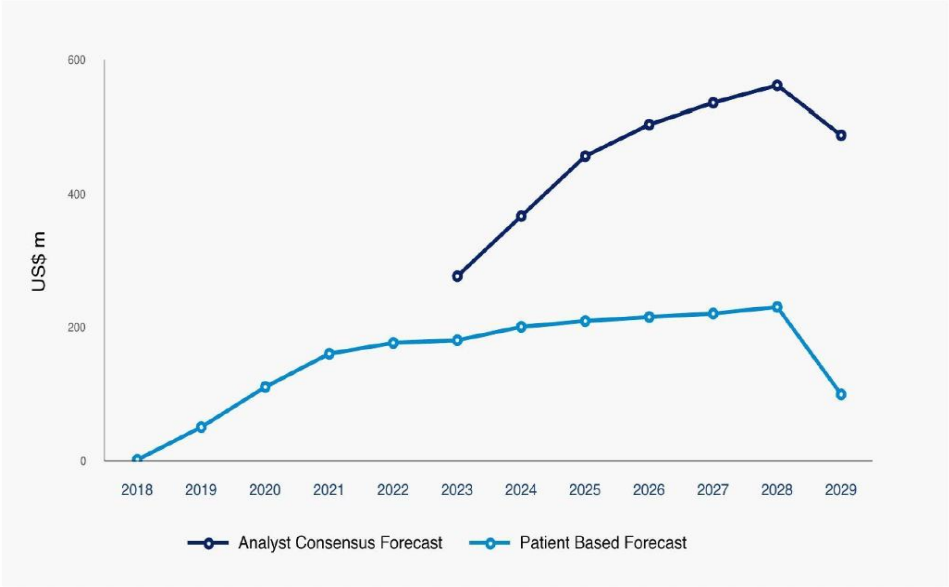
FIGURE 1. NGS TESTING RATES OVER TIME FOR FLATIRON HEALTH PATIENTS WITH aNSCLC AND MBC[1]



aNSCLC, advanced non-small cell lung cancer; mBC, metastatic breast cancer; NGS, next-generation sequencing.

Vanderwalde AM, et al. *J Clin Oncol*. 2021;39(Suppl 28):288.

Projected Larotrectinib Sales



Extracted Date: 06-Nov-2023

“You can be right, but, if you are early, you can be wrong!”

Some annoying rich dude

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“The world of oncology is based on tumor type!”

Marti Raber

Drug	Target	Approval date	Indication	Other Indications	#Trials	#pts	# of Tumor types	mORR (%)	mDOR	Peds (Y/N)	Companion diagnostic (Y/N)
pembro	PD-1	5/23/2017	MSI-High	multiple	5 single arm	149	?	39.6% (31.7-49.9)	>6mths 78% pts	N	N
larotrectinib	NTRK	11/26/2018	NTRK fusion	none	3 single arm	55	12	75% (61-85)	NR (@8.3mths)	Y	N
entrectinib	NTRK	9/15/2019	NTRK fusion	none	3 single arm	54	10	57% (43.2-70.8)	10 mths	Y	N
pembro	PD-1	6/16/2020	TMB-H	multiple	prespecified analysis from multiple phase 2s	102	18	29% (21-39)	NR	Y	Y
dostarlamib	PD-1	8/17/2021	MSI-high	multiple	prespecified analysis from multi-cohort phase 1	327	16	41.6% (34.9-48.6)	34.7mths	N	N
dabrafenib+ trametinib	BRAF+MEK	6/22/2022	BRAFV600E (-CRC)	NSCLC, ATC	3 single arm trials	167	24	41% (33-50) children 25%	DOR ≥6 mths 78% of pts and ≥24 mths for 44% of pts.	Y	N
selpercatinib	RET	9/21/2022	RET FUSION	NSCLC,MTC	prespecified analysis from multi-cohort phase 1/2	41	14	*43.9% (28.5–60.3)* CRC (20%)	*24.5mths*	N	N

MSI = microsatellite instability; mORR = median ORR; mDOR = median DOR.

Key Learning Points

- Tumor-agnostic therapy is here!
  - Targets specific molecular biomarkers across tumor types, regardless of histology, site, or origin
  - Most tumors have the long tail of alterations
  - Increasing use of NGS is identifying these pts
  - Basket trials can rapidly assess activity across multiple histologies
- We now have 9 approvals for 6 indications
  - Trastuzumab deruxtecan (T-DXd) was approved for use in patients with solid tumors characterized by HER2 overexpression
  - Pembrolizumab is approved by the FDA for tumor-agnostic use in patients with MSI-H/dMMR and TMB-H solid tumors
- There are more likely tumor agnostic approvals to come!
- But there are challenges!
  - Prevalence is not always accurate
  - Testing is not as widespread
  - The world of community oncology is still practiced by tumor type

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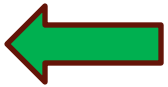
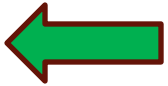
Q&A Session

How Many Indications Are Currently Approved for Tumor-Agnostic Therapy?

A. 5
B. 9
C. 20
D. 6 

How Many Drugs Are Currently Approved for Tumor-Agnostic Therapy?

A. 5
B. 9 
C. 20
D. 6

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Thanks, All Y'all!