康誠生技
Genconn Biotech

GUARDANT

Guardant360
基因檢測服務報告

醫師姓名：江起陸

受檢者姓名：袁金蘭

送檢編號：A1173211

檢測次數：第一次

提醒

基因數據乃屬個人隱私，切勿輕易向任何個人、團體或非您的授權者透漏本報告內容。若您有任何疑慮，歡迎來電洽詢，我們很樂意為您提供更詳細的諮詢服務。若因郵遞錯誤收此檔，請予銷毀，多謝合作。

詳細資訊

康誠生技股份有限公司 客戶服務中心

諮詢時間｜週一～週五 9:00～17:00 （國定假日除外）

諮詢專線｜02-55696099

客服信箱｜service.gb@healthconn.com

REPORTING

Report Date:	OCT-14-2024
Receipt Date:	OCT-10-2024
Collection Date:	OCT-09-2024
Specimen:	Blood
Status:	FINAL

PHYSICIAN

Chi-Lu Chiang
Account: Genconn Biotech Co., LTD
Address: 5F., No. 54, Sec. 1, Jhongsiao E. Rd., Zhongzheng Dist., Beixin Rd, Xindian Dist, Taipei City, 100, Taiwan
Ph: +886 963 820 633 | Fax: N/A
Additional Recipient: N/A

Complete Tumor Response Map on page 2

Summary of Detected Somatic Alterations, Immunotherapy Biomarkers & Associated Treatment Options

KEY ✓ Approved in indication ~ Approved in other indication ⊗ Lack of response

Detected Alteration(s) / Biomarker(s)	Associated FDA-approved therapies	Clinical trial availability (see page 3)	% cfDNA or Amplification
EGFR E746_A750del (Exon 19 deletion)	✓ Afatinib, Amivantamab, Amivantamab+lazertinib, Dacomitinib, Erlotinib, Erlotinib+ramucirumab, Gefitinib, Osimertinib	Yes	13.8%
PTEN Q149Gfs*8	~ Capivasertib	Yes	22.6%
CTNNB1 S45C	None	Yes	11.3%
KRAS L19F	None	Yes	0.1%
TP53 R175H	None	No	11.7%

Comments

Reported by: NT3

Additional Biomarkers

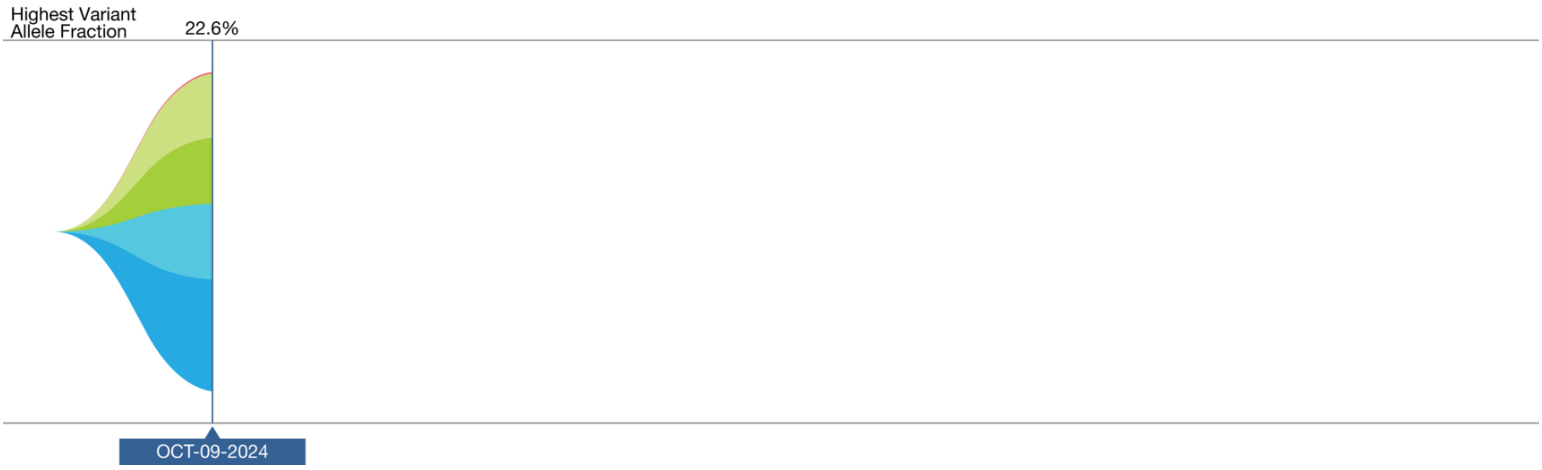
Biomarker	Additional Details
MSI-High	NOT DETECTED

We evaluated this sample for 74 genes, including the following guideline-recommended genes for NSCLC

EGFR(T790M and others) | *ALK* | *ROS1* | *BRAF* | *MET* | *ERBB2*(HER2) | *RET* | *NTRK* | *KRAS*

Guardant360 Tumor Response Map

The Guardant360 Tumor Response Map illustrates the variant allele fraction (% cfDNA) of observed somatic variants at each sample submission. Amplifications are not plotted, and only the first and last five test dates are plotted. Please see the Physician Portal (**portal.guardanthealth.com**) for the Tumor Response Map with all test dates.



Detected Alteration(s) / Biomarker(s)	% cfDNA or Amp
PTEN Q149Gfs*8	22.6%
EGFR E746_A750del (Exon 19 deletion)	13.8%
TP53 R175H	11.7%
CTNNB1 S45C	11.3%
KRAS L19F	0.1%

The table above annotates the variant allele fraction (% cfDNA) detected in this sample, listed in descending order.
§ See definitions section for more detail

Available Clinical Trials (within the same state as the ordering physician)

There may be additional trials not listed here. Visit: **portal.guardanthealth.com** or email **clientservices@guardanthealth.com** with A1173211 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
EGFR E746_A750del	NCT04077463 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer	Phase 1	Kaohsiung, Taiwan Taipei City, Taiwan Tainan, Taiwan Taichung, Taiwan
	NCT05215548 Jin-Shing Chen, M.D., Ph.D.,chenjs@ntu.edu.tw,886-2-2322-0322	Primary Tumor Resection With EGFR TKI for Stage IV NSCLC	Phase 2	Taipei, Taiwan (2)
	NCT05442060 Anna Hu,annahu@obipharma.com,886-2-27866589 x104	To Evaluate OBI-833/OBI-821 in Combination With First-Line Erlotinib in Patients With EGFR-Mutated, Globo H-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	Phase 2	New Taipei City, Taiwan Taoyuan, Taiwan Taichung, Taiwan Taipei, Taiwan (4)
	NCT05801029 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	A Study to Investigate Safety and Efficacy of Osimertinib and Amivantamab in Participants With Non-small Cell Lung Cancer With Common Epidermal Growth Factor Receptor Mutations	Phase 2	Yunlin, Taiwan Taipei City, Taiwan Kaohsiung, Taiwan (2) Taipei, Taiwan (2) Additional trial sites available
	NCT06120140 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Enhanced Dermatological Care to Reduce Rash and Paronychia in Epidermal Growth Factor Receptor (EGRF)-Mutated Non-Small Cell Lung Cancer (NSCLC) Treated First-line With Amivantamab Plus Lazertinib	Phase 2	Kaohsiung City, Taiwan Taipei, Taiwan Taoyuan City, Taiwan Taichung City, Taiwan Additional trial sites available
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
CTNNB1 S45C	NCT04008797 Eisai Inquiry Service,eisai-chiken_hotline@hhc.eisai.co.jp	A Study of E7386 in Combination With Other Anticancer Drug(s) in Participants With Solid Tumor	Phase 1 /Phase 2	Tainan, Taiwan Taoyuan, Taiwan Kao-Hsiung, Taiwan Taipei, Taiwan (2) Additional trial sites available
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
PTEN Q149Gfs*8	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
KRAS L19F	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			

More clinical trial options available at **portal.guardanthealth.com**

Definitions

Deletion (Del): The following alteration was detected in this patient: *EGFR* E746_A750del; *PTEN* Q149Gfs*8. Guardant360 detects short deletions in exons of certain genes (see Table 1), including potential splice site-disrupting events.

Interpretation

Somatic alterations were detected in the circulating cell-free DNA isolated from this patient's blood specimen. These genomic alterations are cancer-associated somatic variants, some of which have been associated with either increased or reduced clinical response to specific treatments. The percentage of altered cell-free DNA circulating (% cfDNA) in blood is related to the unique tumor biology of each patient. Factors that may affect the % cfDNA of detected somatic alterations include tumor growth, turn over, size, heterogeneity, vascularization, disease progression, and treatment.

Method and Limitations

Guardant360 sequences 74 cancer-associated genes to identify somatic alterations. Cell-free DNA (cfDNA) is extracted from plasma, enriched for targeted regions, and sequenced using the Illumina platform and hg19 as the reference genome. All exons are sequenced in some genes; only clinically significant exons are sequenced in other genes. The types of genomic alterations detected by Guardant360 include single nucleotide variants, gene amplifications, fusions, short insertions/deletions (longest detected, 70 base pairs), and splice site disrupting events (see Table 1). Microsatellite Instability (MSI) is assessed for all cancer types by evaluating somatic changes in the length of repetitive sequences on the Guardant360 panel. A "Not Detected" result in samples where the highest % cfDNA is < 0.2% is an inconclusive result because it does not preclude MSI-High status in tissue. MSI status is currently not reported for earlier panel versions. This version of the Guardant360 test is not validated for the detection of other types of genomic alterations, such as complex rearrangements or gene deletions. Certain sample or variant characteristics, such as low cfDNA concentration, may result in reduced analytic sensitivity. Guardant360 cannot discern the source of circulating cfDNA, and for some variants in the range of ~40 to 60% cfDNA, the test cannot easily distinguish germline variants from somatic alterations. Guardant360 is not validated for the detection of germline or de novo variants that are associated with hereditary cancer risk. Tissue genotyping should be considered when plasma genotyping is negative, if clinically appropriate.

Table 1: Genes on the Guardant360 Panel

Guardant360 reports single nucleotide variants, splice site mutations, and insertion and deletion variants (indels) in all clinically relevant exons in 74 genes and reports other variant types in select genes as indicated below.

AKT1	*ALK* #	*APC*	*AR* †	*ARAF*	*ARID1A*	*ATM*	*BRAF* †	*BRCA1*
BRCA2	*CCND1* †	*CCND2* †	*CCNE1* †	*CDH1*	*CDK12*	*CDK4* †	*CDK6* †	*CDKN2A*
CTNNB1	*DDR2*	*EGFR* †	*ERBB2* †	*ESR1*	*EZH2*	*FBXW7*	*FGFR1* †	*FGFR2* † #
FGFR3 #	*GATA3*	*GNA11*	*GNAQ*	*GNAS*	*HNF1A*	*HRAS*	*IDH1*	*IDH2*
JAK2	*JAK3*	*KIT* †	*KRAS* †	*MAP2K1*	*MAP2K2*	*MAPK1*	*MAPK3*	*MET* †
MLH1	*MPL*	*MTOR*	*MYC* †	*NF1*	*NFE2L2*	*NOTCH1*	*NPM1*	*NRAS*
NTRK1 #	*NTRK3*	*PDGFRA* †	*PIK3CA* †	*PTEN*	*PTPN11*	*RAF1* †	*RB1*	*RET* #
RHEB	*RHOA*	*RIT1*	*ROS1* #	*SMAD4*	*SMO*	*STK11*	*TERT* ‡	*TP53*
TSC1	*VHL*							

‡ Guardant360 reports alterations in the promoter region of this gene.

† Guardant360 reports amplifications of this gene.

Guardant360 reports fusion events involving this gene.

About the Test

The Guardant360 assay was developed and its performance characteristics were determined by Guardant Health, Inc. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test may be used for clinical purposes and should not be regarded as investigational or for research only. Guardant Health's clinical reference laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing. The laboratory report should be interpreted in the context of other clinical information and laboratory, pathology, and imaging studies by a qualified medical professional prior to initiating or changing a patient's treatment plan. The selection of any, all, or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) is entirely at the discretion of the treating medical professional. Drug and trial information are based on the diagnosis written on the submitted test request form; this information is not based on any supplemental information provided by the requesting medical professional, including pathology reports or other molecular studies. Some drugs listed in this report may not be approved or cleared by the FDA for the indicated use. Guardant Health makes no endorsement, express or implied, of any product, physician, or procedure contained in this report. This report makes no promises or guarantees that a particular medication will affect (or not affect) the clinical outcome of any patient.

Testing Performed at: Guardant Health

Laboratory Director: Martina Lefterova, MD PhD | CLIA ID: 05D2070300 | CAP #: 8765297 | 505 Penobscot Drive, Redwood City, CA, 94063, USA

Additional information is available

Any therapeutic annotations are based on publicly available information. This information is described in the "Detailed Therapy Results" and "Relevance of Detected Alterations" sections.

Visit **portal.guardanthealth.com** or email **clientservices@guardanthealth.com** with A1173211 in the subject line of the email for:

- Additional clinical trials
- Detailed Therapy Results
- Relevance of Detected Alterations
- References

If you would like to receive this additional information with every Guardant360 report, please call client services at **855.698.8887** to opt-in.

Additional information begins on the next page.

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
EGFR E746_A750del	NCT03574402 Yi-Long Wu, Professor,syylwu@live.cn, 862083827812	Phase II Umbrella Study Directed by Next Generation Sequencing	Phase 2	China
	NCT04077463 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer	Phase 1	Seattle, WA; Detroit, MI; Saint Louis, MO; Philadelphia, PA; Portland, OR; Salt Lake City, UT; Tampa, FL; Fairfax, VA; Boston, MA (2); New York, NY (2); CA (5); Japan (7); China (9); Taiwan (4); Korea, Republic of (4); Italy (5); France (7)
	NCT04922138 Baohui Han, doctor,18930858216@163.com,18930858216	Aumolertinib Adjuvant Therapy of Resectable Stage I EGFRm+ NSCLC With High-grade Patterns	Phase 2	China (2)
	NCT05163028 John Ning, MD,PhD,FAIC,jning@huyabio.com,858-280-1866	A Dose Escalation Study of SHP2 Inhibitor in Patients With Solid Tumors Harboring KRAS of EGFR Mutations	Phase 1	Orlando, FL; Tyler, TX; Plantation, FL; Canton, OH; Fairfax, VA; CA (6); Puerto Rico
	NCT05215548 Jin-Shing Chen, M.D., Ph.D.,chenjs@ntu.edu.tw,886-2-2322-0322	Primary Tumor Resection With EGFR TKI for Stage IV NSCLC	Phase 2	Taiwan (2)
	NCT05442060 Anna Hu,annahu@obipharma.com,886-2-27866589 x104	To Evaluate OBI-833/OBI-821 in Combination With First-Line Erlotinib in Patients With EGFR-Mutated, Globo H-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	Phase 2	Taiwan (7)
	NCT05801029 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	A Study to Investigate Safety and Efficacy of Osimertinib and Amivantamab in Participants With Non-small Cell Lung Cancer With Common Epidermal Growth Factor Receptor Mutations	Phase 2	Glendale, CA; New York, NY; Washington, DC; Sacramento, CA; Beverly Hills, CA; Fairfax, VA; Canada (2); Singapore (3); Hong Kong (4); Taiwan (9); Korea, Republic of (7); Malaysia (6); Thailand (5)
	NCT06041776 Shun Lu, M.D.,shunlu@sjtu.edu.cn,+86 21 2220 0000	Adjuvant Befotertinib in Stage IB-IIIB Non-small Cell Lung Cancer With Positive EGFR Sensitive Mutations	Phase 3	China (3)
	NCT06043973 Degan Lu, Professor,deganlu@126.com, 18753157623	Almonertinib Combined With Anlotinib as First-line Treatment for Advanced Non-small Cell Lung Cance	Phase 3	China
	NCT06120140 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Enhanced Dermatological Care to Reduce Rash and Paronychia in Epidermal Growth Factor Receptor (EGRF)-Mutated Non-Small Cell Lung Cancer (NSCLC) Treated First-line With Amivantamab Plus Lazertinib	Phase 2	Renton, WA; Hinsdale, IL; Westbury, NY; Cleveland, OH; W. Salem, WI; Athens, GA; Chandler, AZ; Reno, NV; Springfield, MO; Fairfax, VA; Flemington, NJ; Wilson, NC; CA (16); Argentina (5); Turkey (8); China (11); Taiwan (5); Korea, Republic of (3); Brazil (11); Malaysia (4); France (3); Germany (6); Spain (9)
CTNNB1 S45C	NCT04008797 Eisai Inquiry Service,eisai-chiken_hotline@hhc.eisai.co.jp	A Study of E7386 in Combination With Other Anticancer Drug(s) in Participants With Solid Tumor	Phase 1 /Phase 2	Oklahoma City, OK; Pasadena, CA; Santa Monica, CA; Los Angeles, CA; Houston, TX; West Palm Beach, FL; La Jolla, CA; Aurora, CO; Sarasota, FL; Nashville, TN; Charleston, SC; Kansas City, MO; New York, NY (2); Dallas, TX (2); Japan (12); Taiwan (6); Korea, Republic of (5); France (21)
	NCT04681248 Leap Therapeutics, Inc.,	Expanded Access Use of DKN-01 for the Treatment of Advanced Solid Tumors		Los Angeles, CA; Milwaukee, WI; Madison, WI; Chicago, IL;

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
	EarlyAccess@leaptx.com,617-714-0360			Birmingham, AL
	NCT04780568 The Ohio State University Comprehensive Cancer Center, OSUCCCClinicaltrials@osumc.edu,800-293-5066	Osimertinib and Tegavivint as First-Line Therapy for the Treatment of Metastatic EGFR-Mutant Non-small Cell Lung Cancer	Phase 1	Columbus, OH
	NCT04851119 See https://clinicaltrials.gov/ct2/show/NCT04851119	Tegavivint for the Treatment of Recurrent or Refractory Solid Tumors, Including Lymphomas and Desmoid Tumors	Phase 1 /Phase 2	Philadelphia, PA; Saint Louis, MO; Minneapolis, MN; New York, NY; Chicago, IL; Orange, CA; San Francisco, CA; Memphis, TN; Los Angeles, CA; Seattle, WA; Houston, TX; Boston, MA; Indianapolis, IN; Atlanta, GA; Pittsburgh, PA; Cincinnati, OH; Washington, DC; Birmingham, AL; Aurora, CO; Ann Arbor, MI
	NCT05919264 Clinical Trial Inquiries, clinicaltrials@fogpharma.com,(857) 259-6305	FOG-001 in Locally Advanced or Metastatic Solid Tumors	Phase 1 /Phase 2	Houston, TX; Saint Louis, MO; Boston, MA; Scottsdale, AZ; New York, NY; New Haven, CT; Portland, OR; San Antonio, TX; Nashville, TN
PTEN Q149Gfs*8	NCT02264678 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Ascending Doses of Ceralasertib in Combination With Chemotherapy and/or Novel Anti Cancer Agents	Phase 1 /Phase 2	Duarte, CA; Philadelphia, PA; Irvine, CA; Los Angeles, CA (2); United Kingdom (5); France (4)
	NCT02407509 Taleen Shakouri, PhD,DDU3808@icr.ac.uk,02034376629	Phase I Trial of VS-6766 Alone and in Combination With Everolimus	Phase 1	United Kingdom (3)
	NCT03065062 Geoffrey Shapiro, MD, Geoffrey_Shapiro@dfci.harvard.edu,617-632-4942	Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors	Phase 1	Boston, MA (3)
	NCT03739710 US GSK Clinical Trials Call Center, GSKClinicalSupportHD@gsk.com,877-379-3718	Platform Trial of Novel Regimens Versus Standard of Care (SoC) in Participants With Non-small Cell Lung Cancer (NSCLC)	Phase 2	Los Angeles, CA; Nashville, TN; Chattanooga, TN; Bronx, NY (2); Germany; Canada (3); Italy (4); France (4); Spain (3)
	NCT05327010 See https://clinicaltrials.gov/ct2/show/NCT05327010	Testing the Combination of the Anti-cancer Drugs ZEN003694 (ZEN-3694) and Talazoparib in Patients With Advanced Solid Tumors, The ComBET Trial	Phase 2	New Haven, CT; Chicago, IL; Sacramento, CA; Houston, TX; Lee's Summit, MO; Duarte, CA; Chapel Hill, NC; North Kansas City, MO; Atlanta, GA; Pittsburgh, PA; La Jolla, CA; Irvine, CA; Aurora, CO; Gainesville, FL; Galveston, TX; Salt Lake City, UT; Trumbull, CT; Lexington, KY; Charlottesville, VA; Kansas City, MO; Bethesda, MD (2); KS (5)
KRAS L19F	NCT02407509 Taleen Shakouri, PhD,DDU3808@icr.ac.uk,02034376629	Phase I Trial of VS-6766 Alone and in Combination With Everolimus	Phase 1	United Kingdom (3)
	NCT05163028 John Ning, MD,PhD,FAIC,jning@huyabio.com,858-280-1866	A Dose Escalation Study of SHP2 Inhibitor in Patients With Solid Tumors Harboring KRAS of EGFR Mutations	Phase 1	Orlando, FL; Tyler, TX; Plantation, FL; Canton, OH; Fairfax, VA; CA (6); Puerto Rico
	NCT05375084 Navire Clinical Operations,NAV1004ct.gov@bridgebio.com,650-391-9740	SHP2 Inhibitor BBP-398 in Combination With Nivolumab in Patients With Advanced Non-Small Cell Lung Cancer With a KRAS Mutation	Phase 1	Philadelphia, PA; Baltimore, MD; Portland, OR; Buffalo, NY; Santa Rosa, CA; Detroit, MI; Cleveland, OH; Springdale, AR; La Jolla, CA;

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
				Hollywood, FL; Tampa, FL; Charleston, SC; Fairfax, VA; Houston, TX (2)
	NCT05585320 IMM1104-101 Study Team, clinicaltrials@immuneering.com,(860) 321-1302	A Phase 1/2a Study of IMM-1-104 in Participants With Previously Treated, RAS-Mutant, Advanced or Metastatic Solid Tumors	Phase 1 /Phase 2	Denver, CO; New York, NY; Chicago, IL; Jacksonville, FL; Santa Monica, CA; Durham, NC; Houston, TX; Duarte, CA; Madison, WI; Rochester, MN; Boston, MA; San Diego, CA; Scottsdale, AZ; Lake Mary, FL; East Syracuse, NY; Nashville, TN; Fairfax, VA
	NCT06162221 Revolution Medicines,CT-inquiries@RevMed.com,(650)779-2300	Study of RAS(ON) Inhibitor Combinations in Patients with Advanced RAS-mutated NSCLC	Phase 1 /Phase 2	Houston, TX; Westbury, NY; Cleveland, OH; Irving, TX; Plantation, FL; New York, NY; Washington, DC; Sacramento, CA; Irvine, CA; Billings, MT; San Francisco, CA; Fairfax, VA; Netherlands; Germany; Italy (2); France (7); Spain (7)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
EGFR E746_A750del (Exon 19 deletion)	ABT-101		Egfr/Her2 inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Head and neck squamous cell carcinoma (HNSCC))
	Afatinib	Gilotrif	Irreversible pan-ErbB kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Lung squamous cell carcinoma, EGFR-mutant NSCLC)
	Amivantamab	Rybrevant	Bispecific anti-Met/Egfr antibody.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (NSCLC with EGFR exon 20 insertion, NSCLC with EGFR exon 19 del /L858R)
	Amivantamab+lazertinib	Rybrevant+Lazcluze	Bispecific anti-Met/Egfr antibody+Egfr tyrosine kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (NSCLC with EGFR exon 19 del/L858R)
	Aumolertinib		Egfr T790M inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC))
	Avitinib		Irreversible mutation-specific Egfr kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Non-Hodgkin lymphoma (NHL))
	BAY2927088		Egfr/Her2 kinase inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC))
	BBP-398		Shp-2 inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	BDTX-1535		Irreversible brain-penetrant fourth generation Egfr inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Glioma)
	Befotertinib		Third generation mutation-specific (T790M, L858R, exon 19 deletion) Egfr tyrosine kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC))
	BLU-945		Fourth generation Egfr inhibitor targeting T790M and T790M/C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	BPI-361175		Fourth generation Egfr inhibitor targeting T790M and T790M/C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	CLN-081		Covalent mutation-specific (L858R, T790M, exon 19 deletion, exon 20 insertion) Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	CM93		Third generation mutation-specific (T790M, L858R, exon 19 deletion) Egfr tyrosine kinase inhibitor.	Phase 1 (Glioblastoma)
	Dacomitinib	Vizimpro	Pan-ErbB family tyrosine kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (EGFR-mutant lung carcinoid, EGFR-mutant lung large cell neuroendocrine carcinoma, EGFR-mutant NSCLC)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	ERAS-601		Shp-2 inhibitor.	Phase 2 (Solid Tumor)
	Erlotinib	Tarceva	Egfr tyrosine kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (EGFR-mutant lung carcinoid, EGFR-mutant lung large cell neuroendocrine carcinoma, NSCLC with EGFR exon 19 del/L858R, Pancreatic carcinoma, EGFR-mutant NSCLC)
	Erlotinib+bevacizumab	Tarceva+Avastin	Egfr tyrosine kinase inhibitor + anti-VEGF-A monoclonal antibody combination.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Lung cancer)
	Erlotinib+ramucirumab	Tarceva+Cyramza	Egfr tyrosine kinase inhibitor + anti-VEGFR-2 monoclonal antibody combination.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (NSCLC with EGFR exon 19 del/L858R)
	ET0038		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	Furmonertinib		Third generation mutation-specific (T790M, L858R, exon 19 deletion) Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	FWD1509		Egfr/Her2 kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	Gefitinib	Iressa	Egfr tyrosine kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (EGFR-mutant lung carcinoid, EGFR-mutant lung large cell neuroendocrine carcinoma, EGFR-mutant NSCLC)
	H002		Fourth generation Egfr inhibitor targeting exon 19del /L858R, T790M, and C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	HBI-2376		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	Hemay022		Egfr tyrosine kinase inhibitor.	Phase 1 (Breast carcinoma (HER2+))
	Icotinib	Conmana	Egfr inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Esophageal carcinoma)
	JIN-A02		Fourth generation Egfr inhibitor targeting T790M and T790M/C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	Lazertinib	Lazcluze	Third generation mutation-specific Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	Lifirafenib		Dual Braf/Egfr inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)
	MCLA-129		Anti-EGFR/c-Met bispecific antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Gastric carcinoma, Head and neck squamous cell carcinoma (HNSCC), Esophageal squamous cell carcinoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status	
	Mobocertinib	Exkivity		Mutation-specific Egfr/Her2 inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (NSCLC with EGFR exon 20 insertion, Lung cancer)
	Modotuximab			Anti-EGFR antibody.	Phase 1 (Gastric carcinoma, Colorectal carcinoma (CRC))
	Nazartinib			Third generation EGFR mutant-specific (T790M, L858R, exon 19 deletion) tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	Neratinib	Nerlynx		Egfr/Her2/ErbB4 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Breast carcinoma (HER2+))
	NX-019			Egfr inhibitor.	Phase 1 (Solid Tumor)
	Olafertinib			Third generation mutation-specific (T790M, L858R, exon 19 deletion) Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	Osimertinib	Tagrisso		Egfr T790M inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (EGFR-mutant lung carcinoid, EGFR-mutant lung large cell neuroendocrine carcinoma, EGFR-mutant NSCLC)
	Pirotinib			ErbB family inhibitor.	Phase 1 (Solid Tumor)
	Poziotinib			Egfr/Her2/ErbB4 kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Gastric carcinoma, Head and neck squamous cell carcinoma (HNSCC), Breast carcinoma, Esophageal squamous cell carcinoma, Colorectal carcinoma (CRC))
	Pyrotinib			Egfr/Her2 kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Breast carcinoma)
	Rezivertinib			Egfr T790M inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC))
	SKLB1028			Egfr/Flt3/c-Abl inhibitor.	Phase 2 (Acute myeloid leukemia (AML))
	Sunvozertinib			Bispecific anti-Egfr/Her2 monoclonal antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Non-Hodgkin lymphoma (NHL))
	TAS2940			Egfr/Her2 kinase inhibitor.	Phase 1 (Solid Tumor)
	TAS3351			Fourth generation Egfr inhibitor targeting T790M and T790M/C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	TAVO412			Anti-c-Met/anti-EGFR/anti-VEGF trispecific antibody.	Phase 1 (Solid Tumor)
	Varlitinib			Egfr/Her2 kinase inhibitor.	Phase 2 (Gastric carcinoma, Hepatocellular carcinoma (HCC), Pancreatic carcinoma, Cholangiocarcinoma)
	WSD0922-FU			Blood-brain barrier penetrable EGFR/EGFRvIII	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Glioblastoma,

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
			inhibitor.	Anaplastic astrocytoma)
	ZN-e4		Egfr T790M inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC))
	Zorifertinib		Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
PTEN Q149Gfs*8	ABTL0812		Inhibitor of mTORC1/mTORC2 /Dhfr.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Pancreatic carcinoma, Endometrial carcinoma)
	Alpelisib	Piqray	p110-alpha inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Breast carcinoma (HR+, HER2-) with a PIK3CA mutation, as determined by a validated test)
	Archexin	Archexin	Akt1 antisense oligonucleotide.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Renal cell carcinoma)
	ARQ 751		Akt inhibitor.	Phase 1 (Solid Tumor)
	AZD8186		p110-beta and p110-delta small molecule inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Breast carcinoma (triple negative), Lung squamous cell carcinoma)
	Buparlisib		PI3K inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Head and neck squamous cell carcinoma (HNSCC), Breast carcinoma)
	Capivasertib	Truqap	Akt inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Breast carcinoma (HR+, HER2-) with a PIK3CA/AKT1 /PTEN mutation)
	CC-115		DNA-PK/dual mTORC1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Glioblastoma, Glioma)
	Copanlisib	Aliqopa	PI3K inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Non-Hodgkin lymphoma (NHL))
	CYH33		p110-alpha-specific small molecule inhibitor.	Phase 1 (Solid Tumor)
	Everolimus	Afinitor	mTOR inhibitor, immunosuppressant.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (TSC associated renal angiomyolipoma and subependymal giant cell astrocytoma, Renal cell carcinoma, Gastrointestinal neuroendocrine carcinoma, Lung carcinoid, Breast carcinoma (hormone receptor +, HER2-), Subependymal giant cell astrocytoma)
	Gedatolisib		Dual PI3K/mTOR inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Breast carcinoma)
	GSK2636771		p110-beta small molecule inhibitor.	Phase 2 (Solid Tumor) Phase 1 (Prostate carcinoma)
	HS-10352		p110-alpha-specific small molecule inhibitor.	Phase 1 (Breast carcinoma)
	Inavolisib	Itovebi	PI3K inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Cancer, Breast carcinoma)
	Ipatasertib		Akt inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Prostate carcinoma, Breast carcinoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	ME-344		Dual mTORC1/mTORC2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Ovarian carcinoma, Small cell lung carcinoma (SCLC))
	MEN1611		PI3K inhibitor.	Phase 2 (Metaplastic breast carcinoma, Colorectal carcinoma (CRC))
	Miransertib		Akt inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	MK-2206		Akt inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Gastric carcinoma, Gallbladder carcinoma, Hepatocellular carcinoma (HCC), Pancreatic carcinoma, Hodgkin lymphoma (HL), Lymphoma, Melanoma, Carcinoid tumor, Prostate carcinoma, Endometrial carcinoma, Renal cell carcinoma, Ovarian carcinoma, Small cell lung carcinoma (SCLC), Adenoid cystic carcinoma, Head and neck carcinoma, Gastroesophageal junction carcinoma, Gastrointestinal neuroendocrine carcinoma, Mucinous colon adenocarcinoma, Breast carcinoma, Chronic lymphocytic leukemia (CLL), Acute myeloid leukemia (AML), Cholangiocarcinoma, Thymic neoplasm, Peritoneal papillary serous carcinoma, Lung cancer, Colorectal carcinoma (CRC), Diffuse large B-cell lymphoma (DLBCL))
	MSC2363318A		Akt1, Akt3, and p70S6K inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma)
	Niraparib	Zejula	PARP inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Prostate carcinoma with BRCA1/2 mutation, Ovarian carcinoma with BRCA1/2 mutation)
	Olaparib	Lynparza	PARP inhibitor.	Phase 2 (Lung adenocarcinoma) FDA Approved in other indications (Pancreatic adenocarcinoma with germline BRCA1/2 mutation, Prostate cancer with HRR gene mutation, Ovarian carcinoma with BRCA1/2 mutation, Breast carcinoma with germline BRCA1/2 mutation)
	Onatasertib		Dual mTORC1/mTORC2 inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Solid Tumor, Bladder neuroendocrine carcinoma, Multiple myeloma (MM), Diffuse large B-cell lymphoma (DLBCL))
	Paxalisib		Dual PI3K/mTOR inhibitor.	Phase 2 (Glioblastoma, Breast carcinoma)
	RLY-2608		p110-alpha-specific small molecule inhibitor.	Phase 1 (Solid Tumor)
	RLY-5836		p110-alpha-specific small molecule inhibitor.	Phase 1 (Solid Tumor)
	RMC-5552		mTORC1-specific inhibitor.	Phase 1 (Solid Tumor)
	Samotolisib		Dual PI3K/mTOR inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Pancreatic carcinoma, Prostate carcinoma)
	Sapanisertib		Dual mTORC1/mTORC2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Uterine carcinosarcoma, Hepatocellular carcinoma (HCC), Lymphoma, Merkel cell carcinoma, Anaplastic thyroid carcinoma, Pancreatic neuroendocrine tumor, Prostate carcinoma, Endometrial carcinoma, Renal cell

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				carcinoma, Ovarian carcinoma, Urothelial carcinoma, Bladder carcinoma, Breast carcinoma, Multiple myeloma (MM), Non-Hodgkin lymphoma (NHL), Lung cancer, Sarcoma, Acute lymphoblastic leukemia (ALL))
	Serabelisib		PI3K inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Endometrial carcinoma, Renal cell carcinoma, Breast carcinoma (triple negative))
	Talazoparib	Talzenna	PARP inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Prostate cancer with HRR gene mutation, Breast carcinoma with germline BRCA1/2 mutation)
	TAS-117		Akt inhibitor.	Phase 2 (Solid Tumor)
	TAS0612		Akt/p70S6K/p90RSK1 multikinase inhibitor.	Phase 1 (Solid Tumor)
	Temsirolimus	Torisel	mTOR inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Renal cell carcinoma)
	TOS-358		p110-alpha-specific small molecule inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Gastric carcinoma, Endometrial carcinoma, Head and neck squamous cell carcinoma (HNSCC), Ovarian carcinoma, Urothelial carcinoma, Breast carcinoma, Cervical carcinoma, Colorectal carcinoma (CRC))
	Triciribine		DNA synthesis and Akt inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Ovarian carcinoma, Breast carcinoma)
	Uprosertib		Akt inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Uveal melanoma, Breast carcinoma, Cervical carcinoma, Acute myeloid leukemia (AML), Multiple myeloma (MM))
	Vistusertib		Dual mTORC1/mTORC2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Meningioma, Small cell lung carcinoma (SCLC), Solid Tumor, Diffuse large B-cell lymphoma (DLBCL))
	WGI-0301		Nanoliposomal Archexin, an Akt1 antisense oligonucleotide.	Phase 1 (Solid Tumor)
KRAS L19F	ASN007		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	ASTX029		ERK1/2 kinase inhibitor.	Phase 2 (Solid Tumor)
	Avutometinib		Dual Raf/MEK kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Uveal melanoma, Ovarian carcinoma)
	BBP-398		Shp-2 inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	BDTX-4933		Braf class 1, 2, and 3 inhibitor.	Phase 1 (Solid Tumor)
	BI 1701963		Pan-K-Ras inhibitor targeting the interaction of K-Ras and SOS-1.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)
	BI 3011441		MEK1,2 inhibitor.	Phase 1 (Solid Tumor)
	Binimetinib	Mektovi	MEK1,2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Melanoma

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				with BRAF V600E/K mutation)
	BMF-219		Covalent menin inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Diabetes)
	Brimarafenib		Braf class 1, 2, and 3 inhibitor.	Phase 2 (Solid Tumor) Phase 1 (Pancreatic ductal adenocarcinoma, Colorectal carcinoma (CRC))
	Cobimetinib	Cotellic	MEK1,2 inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Melanoma with BRAF V600E/K mutation, Histiocytic and dendritic cell neoplasms)
	Defactinib		Focal adhesion kinase (FAK) inhibitor, upstream of MAPK pathway.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Lymphoma, Solid Tumor, Multiple myeloma (MM))
	E6201		MEK1,2, Mekk1, and Flt3 inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Acute myeloid leukemia (AML))
	ERAS-601		Shp-2 inhibitor.	Phase 2 (Solid Tumor)
	ET0038		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	HBI-2376		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	HMPL-295		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	IMM-1-104		MEK1,2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Melanoma, Pancreatic ductal adenocarcinoma)
	JAB-3068		Shp-2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Esophageal carcinoma)
	JAB-3312		Shp-2 inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	JSI-1187		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	KO-2806		Farnesyl transferase inhibitor.	Phase 1 (Solid Tumor)
	LTT462		ERK1/2 kinase inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	LUNA18		Ras peptide inhibitor.	Phase 1 (Solid Tumor)
	Mirdametinib		MEK1,2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Glioma, Neurofibroma, Breast carcinoma, Glioneuronal tumor, Neurofibromatosis type 1, Lung cancer, Colorectal carcinoma (CRC))
	MK-8353		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	MRTX0902		Pan-K-Ras inhibitor targeting the interaction of K-Ras and SOS-1.	Phase 1 (Solid Tumor)
	PF-07284892		Shp-2 inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)
	PF-07799544		MEK Brain Penetrant Inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Glioma, Melanoma, Thyroid carcinoma, Colorectal carcinoma (CRC))

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Pimasertib		MEK1,2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Pancreatic ductal adenocarcinoma, Ovarian carcinoma, Hematologic malignancies, Colorectal carcinoma (CRC))
	RMC-6236		Multispecific Ras inhibitor.	Phase 1 (Solid Tumor)
	RSC-1255		Ras inhibitor.	Phase 1 (Solid Tumor)
	Selumetinib	Koselugo	MEK1,2 inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (NF1-related plexiform neurofibroma)
	SHR7390		MEK1,2 inhibitor.	Phase 1 (Solid Tumor)
	Temuterkib		ERK1/2 kinase inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Pancreatic ductal adenocarcinoma, Solid Tumor)
	Tizaterkib		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Hematologic malignancies)
	TNO155		Shp-2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Colorectal carcinoma (CRC))
	Trametinib	Mekinist	MEK1,2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Melanoma with BRAF V600 mutation)
	Ulixertinib		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Melanoma, Histiocytic and dendritic cell neoplasms, Langerhans cell histiocytosis (LCH), Uveal melanoma, Acute myeloid leukemia (AML), Gastrointestinal carcinoma, Non-Hodgkin lymphoma (NHL), Myelodysplastic Syndrome (MDS))
	Vociprotafib		Shp-2 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Solid Tumor)
CTNNB1 S45C	DKN-01		Anti-DKK-1 monoclonal antibody.	Phase 1 (Solid Tumor)
	E7386		CBP/beta-catenin inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Hepatocellular carcinoma (HCC), Colorectal carcinoma (CRC))
	FOG-001		Beta-catenin polypeptide inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Gastric carcinoma, Gastroesophageal junction carcinoma, Colorectal carcinoma (CRC))
	Tegavivint		Wnt/beta-catenin pathway inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Hepatocellular carcinoma (HCC), Wilms tumor, Ewing sarcoma, Desmoid fibromatosis)

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
EGFR E746_A750del	The presence of an EGFR abnormality (mutation, amplification, or overexpression) can result in an overabundance or overactivity of Egfr protein, which can lead to excessive proliferation. (1).	The presence of a sensitizing EGFR mutation in a tumor is the strongest biological predictor of sensitivity to an Egfr tyrosine kinase inhibitor (TKI). Compared with conventional chemotherapy, Egfr TKIs have been shown to improve progression-free survival in non-small cell lung cancer patients whose tumors harbor EGFR mutations. (2-5). The Egfr TKIs erlotinib, afatinib, gefitinib, osimertinib, and dacomitinib, as well as the combination of amivantamab plus lazertinib, have been approved by the FDA for the treatment of non-small cell lung cancer (NSCLC) with exon 19 deletion or L858R EGFR mutations; osimertinib has additionally been approved for the treatment of NSCLC with EGFR T790M. (2,5-14). Afatinib has additionally been FDA-approved for the treatment of NSCLC with S768I, L861Q, and/or G719X mutations. (15). The combination of erlotinib and ramucirumab as well as osimertinib plus platinum-based chemotherapy have been FDA-approved for the treatment of metastatic NSCLC patients with tumors harboring an EGFR exon 19 deletion or the exon 21 L858R mutation. (16-18). Amivantamab in combination with carboplatin and pemetrexed has been FDA-approved for the treatment of adult patients with locally advanced or metastatic NSCLC harboring EGFR Exon 19 deletions or Exon 21 L858R substitution mutations whose disease has progressed on or after treatment with an EGFR TKI. (12,19). Amivantamab has also been approved by the FDA for NSCLC patients with EGFR exon 20 insertions, whose disease has progressed on or after platinum-based chemotherapy and as frontline therapy in combination with carboplatin and pemetrexed. The accelerated FDA approval of mobocertinib for NSCLC patients with EGFR exon 20 insertions has been withdrawn due to lack of progression-free survival benefit in the confirmatory Phase 3 trial. (20-23). Studies have reported non-squamous NSCLC patients with metastatic disease and tumors harboring an EGFR exon 19 deletion or L858R mutation to be sensitive to osimertinib, erlotinib, afatinib, gefitinib, dacomitinib, and the combination of erlotinib plus ramucirumab. (2,5-7,11,16,24). Less	Some patients with EGFR-mutant NSCLC exhibit resistance to Egfr inhibition; resistance has been associated with insertions in EGFR exon 20, the T790M mutation in EGFR, and amplification of either MET or ERBB2. (26-30). Third generation irreversible Egfr TKIs that target the EGFR T790M mutation have shown efficacy in T790M-mutant NSCLC, including osimertinib, which has received approval by the FDA, EMA, and PMDA for the treatment of EGFR T790M-mutant metastatic NSCLC. (31-35). Several studies have reported that resistance to Egfr TKIs in NSCLC is mediated by the transformation of NSCLC cell types to those of SCLC with neuroendocrine features. (36-39).

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
		common activating EGFR mutations have variable sensitivity to EGFR tyrosine kinase inhibitors. [25].	
PTEN Q149Gfs*8	Loss of PTEN (through mutation or deletion) can lead to uncontrolled cell growth and suppression of apoptosis. [40]. PTEN haploinsufficiency has been associated with tumorigenesis in some tumor types, including astrocytoma and prostate cancer. [41-44]. PTEN germline mutations are found in several cancer-predisposition syndromes, such as Cowden syndrome and Proteus syndrome. [45]. Loss of Pten protein expression has been associated with higher stage, lymph node metastases, and poorly differentiated disease in NSCLC patients. [46-51]. Deletion of PTEN has been shown to lead to the formation of lung squamous cell carcinoma tumors in preclinical studies. [52,53].	Because PTEN negatively regulates the PI3K/Akt/mTOR pathway, PTEN loss or mutation leads to activation of the PI3K pathway and may therefore predict sensitivity to inhibitors of the PI3K/Akt /mTOR pathway. [54]. The PI3K inhibitors alpelisib and copanlisib, the Akt inhibitor capivasertib, and the mTOR inhibitors everolimus and temsirolimus have been approved in specific cancer indications. These and other PI3K, Akt, and mTOR inhibitors, as well as dual PI3K/mTOR inhibitors are also currently in clinical trials, alone or in combination with other therapies. [55-59]. The Akt inhibitor capivasertib has been approved by the FDA in combination with fulvestrant for the treatment of adult patients with hormone receptor positive, Her2 negative locally advanced or metastatic breast cancer with PIK3CA /AKT1/PTEN alterations as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy. [60]. In addition, preclinical studies have shown that PTEN-deficient tumors may be sensitive to PARP inhibitors, and PARP inhibitors are in clinical trials for patients with PTEN-deficient tumors. [61-68].	Preclinical studies have associated decreased expression of Pten with gefitinib and erlotinib resistance in EGFR-mutant NSCLC cell lines. [69-71]. Mutation of PTEN has been reported to be associated with a low objective response rate (ORR) to Egfr tyrosine kinase inhibitors in lung adenocarcinomas harboring EGFR mutations, with 7.3% ORR in PTEN-mutated cases compared to 70.9% ORR in wild-type PTEN lung adenocarcinomas. [72].
CTNNB1 S45C	CTNNB1 can act as an oncogene and altered expression of beta-catenin can lead to abnormal signaling in various diseases, including modulation of gene transcription to drive cancer initiation, progression, survival, and relapse. [73]. Beta-catenin expression has been reported to be a marker for epithelial-to-mesenchymal transition (EMT) in non-small cell lung carcinoma (NSCLC) cells. [74]. In addition, one study analyzing 143 NSCLC cases reported that CTNNB1 promoter hypermethylation was correlated with loss of beta-catenin expression, positive lymph node metastasis, and higher TNM staging. [75].	CTNNB1 mutations, particularly those in exon 3, have been associated with increased beta-catenin protein stability and activation of the Wnt pathway. [76-81]. At the present time, there are no approved therapies that target CTNNB1 mutation, however, beta-catenin/Wnt pathway inhibitors are under preclinical and clinical investigation. [82-87].	Beta-catenin activation has been associated with immune evasion and resistance to checkpoint inhibitors in preclinical cancer models. [88-93]. Hyperactivation of the Wnt/beta-catenin pathway may confer resistance to inhibitors of PI3K and Akt. [94]. Activation or increased expression of beta-catenin has been suggested to play a role in resistance to a variety of agents in NSCLC cell lines, including gemcitabine, cisplatin, or gefitinib. [74,96].
KRAS L19F	The KRAS gene is one of the most commonly mutated genes in human	Many of the current attempts to target K-Ras are directed against its	In some cancer types, such as colorectal cancer (CRC) and non-small

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
	malignancies, with high incidences in pancreatic, colorectal, and lung cancers. [97-99]. KRAS mutation, particularly G12C, has been associated with smoking in NSCLC patients; additionally, KRAS mutations have also been associated with adenocarcinoma histology and are generally mutually exclusive with EGFR mutations and ALK rearrangements. [100-112]. Studies analyzing KRAS mutation association with PD-L1 expression in NSCLC patients have reported mixed results; while two older large meta-analyses have reported no association or negative association, smaller studies and one newer large meta-analysis have reported a positive association. [105,112-127].	downstream signaling pathways, Raf /MEK/ERK and PI3K/Akt/mTOR. [128,129]. Clinical studies have suggested limited efficacy of MEK inhibitors in KRAS mutant tumors; however, combinations of MEK inhibitors with other targeted therapies may still be relevant. [130-139]. Other clinical approaches are being investigated preclinically and clinically in the context of KRAS-mutant tumors, including FAK and Shp-2 inhibitors. [140-145]. In addition, inhibitors specifically targeting KRAS G12C and cell-based therapies targeting KRAS G12V and G12D are being investigated clinically and preclinically. [146-149]. Sotorasib and adagrasib have been FDA-approved in patients with locally advanced or metastatic non-small cell lung carcinoma harboring a KRAS G12C mutation, as determined by an FDA-approved test, following treatment with at least one prior systemic therapy. [150-154]. In addition, combinations of adagrasib or sotorasib with cetuximab or panitumumab have been reported to provide clinical benefit in CRC patients with KRAS G12C mutation. [155-158]. Adagrasib plus cetuximab has been FDA-approved for treatment of adults with KRAS G12C-mutated locally advanced or metastatic colorectal cancer, as determined by an FDA-approved test, who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy. [157,159]. Studies analyzing KRAS mutation association with clinical benefit of PD-1/PD-L1 inhibitors to NSCLC patients have reported mixed results, with some studies reporting no significant association while other studies have reported that KRAS mutation correlated with improved clinical outcome of NSCLC patients treated with PD-1/PD-L1 inhibitors. [115,160-163].	cell lung cancer (NSCLC), activating KRAS mutations and KRAS amplification have been associated with resistance to Egfr-targeted therapies. [164-172]. While some studies have suggested that KRAS mutation status may predict lack of response to the Egfr inhibitors erlotinib and gefitinib in NSCLC patients, a retrospective study suggests that there is no significant difference in response to Egfr tyrosine kinase inhibitors among NSCLC patients with KRAS wild-type and KRAS mutation, when EGFR mutation status is included in the analysis. [173-177]. In addition, KRAS mutations have been reported in 1-3% of EGFR-mutant NSCLC patients following emergence of resistance to osimertinib. Treatment with K-ras inhibitors sotorasib or adagrasib in combination with osimertinib may be an effective strategy in patients with KRAS G12C mutation. [178-180]. Case studies of NSCLC patients harboring ALK mutations or EML4-ALK fusions have reported the emergence of KRAS alterations upon acquired resistance to crizotinib, demonstrating a role for KRAS in crizotinib resistance in NSCLC. [181-185]. Secondary KRAS mutations have also been reported in case studies of NSCLC patients with KRAS G12C following emergence of resistance to sotorasib or adagrasib. [186-189].
TP53 R175H	Loss of tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers. [190]. Carriers of a germline mutation in TP53 have Li-Fraumeni Syndrome, an inherited cancer syndrome resulting in multiple tumors in early adulthood, including breast cancer, brain tumors, and leukemias. [191-193]. Expression of p53 in normal	At present, there are no approved therapies targeting TP53 alterations, despite their high prevalence in cancer. Therapeutic approaches under investigation include gene therapy for TP53 and (dendritic cell-based) TP53 vaccines. [208-210]. Inhibition of components of the DNA damage checkpoint, including Wee1, has been reported to enhance the activity of	Mutations in TP53 may increase resistance to ionizing radiation therapy. [220,221].

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
	cells is low; however, TP53 alterations, including those that result in loss of p53 tumor suppressor function, may lead to stabilization and increased expression of p53, particularly in the nucleus, and several studies have shown that it may have oncogenic gain-of-function effects. [194-198]. TP53 alterations are believed to be early events in NSCLC, preceding lymph node metastasis. [199]. TP53 mutation and expression of p53 have been correlated with the lung squamous cell carcinoma subtype, and p53 expression in lung squamous cell carcinoma has also been associated with disease stage and higher grade tumors. [200-203]. TP53 mutation has been associated with PD-L1 expression and T-cell infiltration in lung adenocarcinoma samples. [121,126,204-206]. TP53 mutations have been significantly associated with the development of distant metastases after diagnosis in early-stage NSCLC in a cohort of 759 patients. [207].	DNA-damaging agents in preclinical cancer models with deficiency of p53 function. [211-213]. Clinical trials of the Wee1 inhibitor adavosertib (MK-1775) are currently underway for patients with solid tumors and hematologic malignancies. Studies have reported Aurora kinase A to be activated in cells harboring TP53 mutation, and Aurora kinase A and B inhibitors have been reported to activate wild-type p53 in cellular assays; thus, tumors retaining a wild-type TP53 allele may benefit from Aurora kinase inhibitors. [214-219].	

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