REPORTING

Report Date:	JAN-17-2024
Receipt Date:	JAN-12-2024
Collection Date:	JAN-11-2024
Specimen:	Blood
Status:	FINAL

PHYSICIAN

Chih-Hsueh Chen
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Address: F15., No 207-5 Sec 3, Beixin Rd, Xindian Dist, New Taipei City, 23143, Taiwan
Ph: +886 963 820 633 | Fax: N/A
Additional Recipient: N/A

Complete Tumor Response Map on page 3

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 4)	% cfDNA or Amplification
EGFR L858R	✓ Afatinib, Dacomitinib, Erlotinib, Erlotinib+ramucirumab, Gefitinib, Osimertinib	Yes	13.9%
MET Amplification	~ Capmatinib, Crizotinib, Tepotinib	Yes	High (+++)
TP53 P278H	None	Yes	16.7%
TP53 R110fs	None	Yes	0.2%
EGFR Amplification	None	Yes	Low (+)

Variants of Uncertain Clinical Significance
ALK R1209L (5.3%), *EGFR* A613T (0.8%)
The functional consequences and/or clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Comments

Reported by: DO

Additional Biomarkers

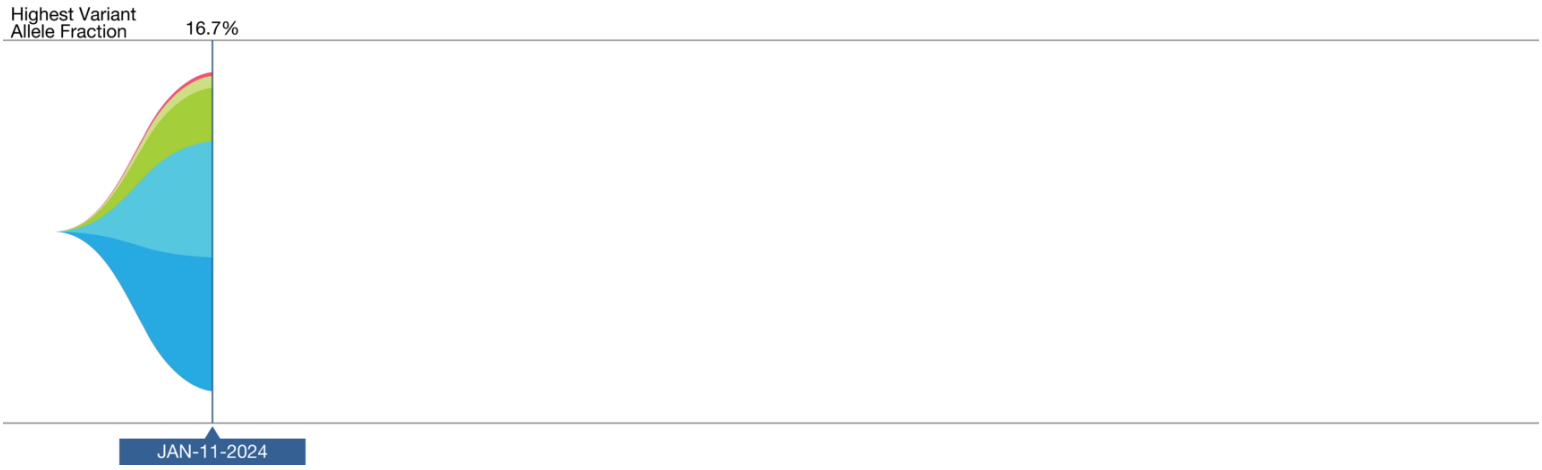
Biomarker	Additional Details
MSI-High	NOT DETECTED

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	
TP53 P278H	16.7%	
EGFR L858R	13.9%	
ALK R1209L	5.3%	Variants of Uncertain Clinical Significance §
EGFR A613T	0.8%	Variants of Uncertain Clinical Significance §
TP53 R110fs	0.2%	
MET Amplification Amplifications not graphed above	High (+++) Plasma Copy Number 3.9	
EGFR Amplification Amplifications not graphed above	Low (+) Plasma Copy Number 2.2	

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 A0941729 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
EGFR L858R	NCT03778229 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib	Phase 2	Kaohsiung, Taiwan Taipei City, Taiwan New Taipei, Taiwan Taipei, Taiwan (2) Additional trial sites available
	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
	NCT05261399 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment	Phase 3	Kaohsiung City, Taiwan Taipei City, Taiwan Chiayi, Taiwan Taipei, Taiwan Additional trial sites available
	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)
	NCT05663866 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Premedication to Reduce Amivantamab Associated Infusion Related Reactions	Phase 2	ChangHua, Taiwan Kaohsiung, Taiwan Taipei City, Taiwan Tainan City, Taiwan Additional trial sites available
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
MET Amplification	NCT03778229 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib	Phase 2	Kaohsiung, Taiwan Taipei City, Taiwan New Taipei, Taiwan Taipei, Taiwan (2) Additional trial sites available
	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
	NCT05261399 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment	Phase 3	Kaohsiung City, Taiwan Taipei City, Taiwan Chiayi, Taiwan Taipei, Taiwan Additional trial sites available
	NCT05663866 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Premedication to Reduce Amivantamab Associated Infusion Related Reactions	Phase 2	ChangHua, Taiwan Kaohsiung, Taiwan Taipei City, Taiwan Tainan City, Taiwan Additional trial sites available
	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

Alteration	Trial ID / Contact	Title	Phase	Site(s)
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
TP53 P278H	NCT04768868 Jian Wang,Jian.wang@impacttherapeutics.com,+86 18613056501	The Safety and Pharmacokinetics Preliminary Efficacy of IMP7068 in Patients With Advanced Solid Tumors	Phase 1	Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan Tainan, Taiwan (2)
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
TP53 R110fs	NCT04768868 Jian Wang,Jian.wang@impacttherapeutics.com,+86 18613056501	The Safety and Pharmacokinetics Preliminary Efficacy of IMP7068 in Patients With Advanced Solid Tumors	Phase 1	Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan Tainan, Taiwan (2)
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
EGFR Amplification	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
	NCT05099172 Bayer Clinical Trials Contact,clinical-trials-contact@bayer.com,(+)1-888-84 22937	First in Human Study of BAY2927088 in Participants Who Have Advanced Non-small Cell Lung Cancer (NSCLC) With Mutations in the Genes of Epidermal Growth Factor Receptor (EGFR) and/or Human Epidermal Growth Factor Receptor 2 (HER2)	Phase 1	Taipei, Taiwan Tainan, Taiwan Taoyuan, 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)
	NCT05647122 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	First in Human Study of AZD9592 in Solid Tumors	Phase 1	Taipei City, Taiwan Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan
	NCT05663866 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Premedication to Reduce Amivantamab Associated Infusion Related Reactions	Phase 2	ChangHua, Taiwan Kaohsiung, Taiwan Taipei City, Taiwan Tainan City, Taiwan Additional trial sites available
	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

Variants of Uncertain Clinical Significance: The functional consequences and/or clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Amplification: Guardant360 detects amplifications in the genes listed in Table 1. Gene amplification results in increased copies of the gene present in the cfDNA. The reported absolute copy number value represents the average copy number for the detected gene that was detected in circulating cfDNA. With the exception of sex-linked genes such as *AR*, 2 copies are expected in the absence of amplification. As the absolute number of copies in circulation is dependent on both tumor fraction and the magnitude of the tumor amplification, amplifications are reported on a semi-quantitative scale.
For *CCNE1*, *EGFR* and *FGFR1*, three levels are reported:
Low (+): Amplification magnitude is below the 50th percentile of amplifications detected by Guardant360.
Medium (++): Amplification magnitude is between the 50th and 90th percentiles.
High (+++): Amplification magnitude is above the 90th percentile.

For *BRAF*, *CCND1*, *CCND2*, *CDK4*, *CDK6*, *ERBB2*, *FGFR2*, *KIT*, *KRAS*, *MET*, *PDGFRA*, *RAF1*, *MYC*, *PIK3CA* and *AR*, two levels are reported:
Medium (++): Amplification magnitude is below the 50th percentile of amplifications detected by Guardant360.
High (+++): Amplification magnitude is above the 50th percentile.

Deletion (Del): The following alteration was detected in this patient: *TP53* R110fs. 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.

Amplification was detected in the circulating cell-free DNA isolated from this patient's blood specimen for the annotated gene(s). Unlike tissue-based gene amplification tests (e.g. IHC or FISH), Guardant360 assesses the total representation of a given gene in all circulating cell-free DNA present in the patient's blood sample including material derived from the tumor and healthy tissue alike. As such, the absolute level of amplification present in the blood depends both on the tumor-derived cfDNA content and on the degree of amplification within that fraction and cannot be inferred from bulk cfDNA interrogation. For example, a positive Guardant360 test could represent a small population of cells with extremely high levels of the detected gene amplification. Alternatively, it could represent a large population of cells with low to medium levels of the detected gene amplifications. The exact correlation between amplification detected by Guardant360 compared to IHC or FISH and how each test differentially guides patient management is an area of active investigation.

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 fusion events involving this gene.

† Guardant360 reports amplifications of 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 A0941729 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 L858R	NCT03778229 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib	Phase 2	Los Angeles, CA; Brooklyn, NY; Seattle, WA; Rochester, MN; Pittsburgh, PA; La Jolla, CA; Washington, DC; Sacramento, CA; Canada (5); Vietnam (2); Taiwan (9); Denmark (3); Brazil (7); Italy (8); Chile (2); Spain (6); India (3)
	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 (3); New York, NY (2); CA (5); Puerto Rico; Japan (7); China (13); Taiwan (4); Korea, Republic of (4); Italy (5); France (7); Germany (8); Spain (8)
	NCT05261399 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment	Phase 3	Orlando, FL; Boston, MA; La Jolla, CA; New York, NY; New Brunswick, NJ; Orange City, FL; Nashville, TN; Honolulu, HI; Austria; Russian Federation (2); Singapore (2); Hong Kong (3); Malaysia (3); Thailand (6); Greece (8); Vietnam (5); China (26); Poland (4); Korea, Republic of (8); Brazil (17); France (16); Chile (3); Bulgaria (4); Argentina (10); Philippines (9); Japan (23); United Kingdom (4); Switzerland (4); Spain (16); Canada (4); Turkey (6); Belgium (7); Taiwan (9); Italy (17); Israel (6); Australia (4); Germany (10)
	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)
	NCT05507606 See https://clinicaltrials.gov/ct2/show/NCT05507606	Study of Osimertinib+Bevacizumab+Chemotherapy for EGFR+ Advanced Non-Small Cell Lung Cancer With Concurrent Mutations	Phase 2	China
	NCT05642572 See https://clinicaltrials.gov/ct2/show/NCT05642572	Comparing Combinations of Targeted Drugs for Advanced Non-Small Cell Lung Cancer That Has EGFR and MET Gene Changes (A Lung-MAP Treatment Trial)	Phase 2	Sunnyvale, CA; Brewer, ME; Gainesville, GA; Palo Alto, CA; Cape Girardeau, MO; Voorhees, NJ; Sylvania, OH; Modesto, CA; Moorestown, NJ; WI (6); IL (18)
	NCT05663866 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Premedication to Reduce Amivantamab Associated Infusion Related Reactions	Phase 2	Renton, WA; Fountain Valley, CA; Fairfax, VA; Taiwan (7); Korea, Republic of (6); France (6); Spain (14)
	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
MET Amplification	NCT03778229 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib	Phase 2	Los Angeles, CA; Brooklyn, NY; Seattle, WA; Rochester, MN; Pittsburgh, PA; La Jolla, CA; Washington, DC; Sacramento, CA; Canada (5); Vietnam (2); Taiwan (9); Denmark (3); Brazil (7); Italy (8); Chile (2); Spain (6); India (3)

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
	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 (3); New York, NY (2); CA (5); Puerto Rico; Japan (7); China (13); Taiwan (4); Korea, Republic of (4); Italy (5); France (7); Germany (8); Spain (8)
	NCT05009836 Lu Chen,Luc@hutch-med.com,+86 021 -20673000 x5014	Clinical Study on Savolitinib + Osimertinib in Treatment of EGFRm+/MET+ Locally Advanced or Metastatic NSCLC	Phase 3	China
	NCT05120960 Barbara O'Brien, MD, bjobrien@mdanderson.org,(713) 794-4380	A Phase 1a/1b Study to Determine the Recommended Phase 2 Dose, of Tepotinib in Participants With MET Alterations and Brain Tumors	Phase 1	Houston, TX
	NCT05261399 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment	Phase 3	Orlando, FL; Boston, MA; La Jolla, CA; New York, NY; New Brunswick, NJ; Orange City, FL; Nashville, TN; Honolulu, HI; Austria; Russian Federation (2); Singapore (2); Hong Kong (3); Malaysia (3); Thailand (6); Greece (8); Vietnam (5); China (26); Poland (4); Korea, Republic of (8); Brazil (17); France (16); Chile (3); Bulgaria (4); Argentina (10); Philippines (9); Japan (23); United Kingdom (4); Switzerland (4); Spain (16); Canada (4); Turkey (6); Belgium (7); Taiwan (9); Italy (17); Israel (6); Australia (4); Germany (10)
	NCT05642572 See https://clinicaltrials.gov/ct2/show/NCT05642572	Comparing Combinations of Targeted Drugs for Advanced Non-Small Cell Lung Cancer That Has EGFR and MET Gene Changes (A Lung-MAP Treatment Trial)	Phase 2	Sunnyvale, CA; Brewer, ME; Gainesville, GA; Palo Alto, CA; Cape Girardeau, MO; Voorhees, NJ; Sylvania, OH; Modesto, CA; Moorestown, NJ; WI (6); IL (18)
	NCT05663866 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Premedication to Reduce Amivantamab Associated Infusion Related Reactions	Phase 2	Renton, WA; Fountain Valley, CA; Fairfax, VA; Taiwan (7); Korea, Republic of (6); France (6); Spain (14)
	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	Canada; Singapore (3); Hong Kong (4); Taiwan (9); Korea, Republic of (7); Malaysia (6); Thailand (5)
TP53 P278H	NCT02769962 Danielle F Pinkiert, R.N.,danielle.pinkiert@nih.gov,(240) 858-7566	Trial of EP0057, a Nanoparticle Camptothecin With Olaparib in People With Relapsed /Refractory Small Cell Lung Cancer	Phase 1 /Phase 2	Bethesda, MD
	NCT03968653 Debiopharm International S.A, clinicaltrials@debiopharm.com,+41 21 321 01 11	Study of Oral Debio 0123 in Combination With Carboplatin in Participants With Advanced Solid Tumors	Phase 1	Spain; Netherlands (3)
	NCT04768868 Jian Wang,Jian.wang@impacttherapeutics.com,+86 18613056501	The Safety and Pharmacokinetics Preliminary Efficacy of IMP7068 in Patients With Advanced Solid Tumors	Phase 1	Louisville, KY; Boston, MA; Atlanta, GA; Dallas, TX; Fairway, KS; San Antonio, TX; China (4); Taiwan (5)
	NCT04869475 Min Shi, MD & Ph. D,sm11998@rjh.com.cn,+86-21-64370045	Arsenic Trioxide in Refractory Solid Tumors With Rescuable p53 Mutation	Phase 2	China

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
	NCT05109975 Debiopharm International S.A, clinicaltrials@debiopharm.com,+41 21 321 01 11	A Study to Evaluate Safety and Preliminary Anti-tumor Activity of Debio 0123 as Monotherapy in Adult Participants With Advanced Solid Tumors	Phase 1	Grand Rapids, MI; San Antonio, TX; Switzerland (2)
	NCT05489731 li zhang, professor,zhangli6@mail.sysu.edu.cn,13902282893	VIC-1911 Combined With Osimertinib for EGFR -Mutant Non-small Cell Lung Cancer	Phase 1	China
TP53 R110fs	NCT02769962 Danielle F Pinkiert, R.N.,danielle.pinkiert@nih.gov,(240) 858-7566	Trial of EP0057, a Nanoparticle Camptothecin With Olaparib in People With Relapsed /Refractory Small Cell Lung Cancer	Phase 1 /Phase 2	Bethesda, MD
	NCT03968653 Debiopharm International S.A, clinicaltrials@debiopharm.com,+41 21 321 01 11	Study of Oral Debio 0123 in Combination With Carboplatin in Participants With Advanced Solid Tumors	Phase 1	Spain; Netherlands (3)
	NCT04768868 Jian Wang,Jian.wang@impacttherapeutics.com,+86 18613056501	The Safety and Pharmacokinetics Preliminary Efficacy of IMP7068 in Patients With Advanced Solid Tumors	Phase 1	Louisville, KY; Boston, MA; Atlanta, GA; Dallas, TX; Fairway, KS; San Antonio, TX; China (4); Taiwan (5)
	NCT04869475 Min Shi, MD & Ph. D,sm11998@rjh.com.cn,+86-21-64370045	Arsenic Trioxide in Refractory Solid Tumors With Rescuable p53 Mutation	Phase 2	China
	NCT05109975 Debiopharm International S.A, clinicaltrials@debiopharm.com,+41 21 321 01 11	A Study to Evaluate Safety and Preliminary Anti-tumor Activity of Debio 0123 as Monotherapy in Adult Participants With Advanced Solid Tumors	Phase 1	Grand Rapids, MI; San Antonio, TX; Switzerland (2)
	NCT05489731 li zhang, professor,zhangli6@mail.sysu.edu.cn,13902282893	VIC-1911 Combined With Osimertinib for EGFR -Mutant Non-small Cell Lung Cancer	Phase 1	China
EGFR Amplification	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 (3); New York, NY (2); CA (5); Puerto Rico; Japan (7); China (13); Taiwan (4); Korea, Republic of (4); Italy (5); France (7); Germany (8); Spain (8)
	NCT05099172 Bayer Clinical Trials Contact,clinical-trials-contact@bayer.com,(+)1-888-84 22937	First in Human Study of BAY2927088 in Participants Who Have Advanced Non-small Cell Lung Cancer (NSCLC) With Mutations in the Genes of Epidermal Growth Factor Receptor (EGFR) and/or Human Epidermal Growth Factor Receptor 2 (HER2)	Phase 1	Houston, TX; Detroit, MI; Bethesda, MD; Boston, MA; Atlanta, GA; Nashville, TN; Fairfax, VA; Gilbert, AZ; Duarte, CA (2); Singapore (2); Hong Kong (2); Japan (8); Portugal (2); Spain (6); Netherlands (2); Belgium (2); China (12); Taiwan (4); Poland (2); Korea, Republic of (6); Brazil (3); Italy (8); Israel (2); France (5)
	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)
	NCT05498428 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	A Study of Amivantamab in Participants With Advanced or Metastatic Solid Tumors Including Epidermal Growth Factor Receptor (EGFR)-Mutated Non-Small Cell Lung Cancer	Phase 2	Orlando, FL; Westwood, KS; Saint Louis, MO; Stanford, CA; Winston-Salem, NC; Orange, CA; New Brunswick, NJ; Charlotte, NC; Boca Raton, FL; Hackensack, NJ; Miami

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
				Beach, FL; Seattle, WA; Boston, MA; La Jolla, CA; Washington, DC; East Syracuse, NY; Salt Lake City, UT; Warrensville Heights, OH; Tampa, FL; Fairfax, VA; Mayfield Heights, OH; Cleveland, OH (2); Japan (6); China (18); Korea, Republic of (5); Brazil (9); United Kingdom (7); Italy (5); Malaysia (4); Israel (5); France (6); Germany (5); Spain (14)
	NCT05647122 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	First in Human Study of AZD9592 in Solid Tumors	Phase 1	Providence, RI; Houston, TX; Duarte, CA; Mineola, NY; Milford, MA; Philadelphia, PA; Irvine, CA; Baltimore, MD; Fairfax, VA; North Haven, CT; New York, NY (2); Malaysia; Canada (2); Japan (2); China (5); Taiwan (4); Korea, Republic of (4); Italy (4); France (2); Australia (2); Spain (3)
	NCT05663866 Study Contact,Participate-In-This-Study@its.jnj.com,844-434-4210	Premedication to Reduce Amivantamab Associated Infusion Related Reactions	Phase 2	Renton, WA; Fountain Valley, CA; Fairfax, VA; Taiwan (7); Korea, Republic of (6); France (6); Spain (14)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
MET Amplification	ABBV-400		anti-Met antibody-drug conjugate.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	ABN401		Met inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)
	AL2846		Met small molecule inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Altiratinib		Met/VEGFR/TIE2/Trk inhibitor.	Phase 1 (Solid Tumor)
	AMG 337		Met and Ron inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Solid Tumor)
	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)
	AZD9592		Bispecific anti-Met/Egfr antibody drug conjugate.	Phase 1 (Solid Tumor)
	Bozitinib		Met inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Glioma, Solid Tumor)
	BPI-9016M		Met/Axl inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	Cabozantinib	Cometriq	Multi-kinase inhibitor with targets including Met, Ret, VEGFR-2, Tie2, and Kit.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Thyroid carcinoma, well differentiated, Hepatocellular carcinoma (HCC), Renal cell carcinoma, Thyroid medullary carcinoma)
	Capmatinib	Tabrecta	Met inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (NSCLC with a MET exon 14 skipping mutation)
	Crizotinib	Xalkori	Alk/Met/Ros1 kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (ALK-positive inflammatory myofibroblastic tumor, ALK- and ROS1-rearranged NSCLC, Anaplastic large cell lymphoma, ALK positive)
	Elzovantinib		Met/Src/CSF-1R inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Emibetuzumab		Anti-Met monoclonal antibody.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	Ficlatuzumab		Anti-HGF monoclonal antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Pancreatic carcinoma, Head and neck squamous cell carcinoma (HNSCC))
	Glesatinib		Multitargeted small molecule kinase inhibitor (Met/Tie-2/VEGFR1, 2,3/Ron).	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Lung cancer)
	Glumetinib		Met inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)
	GST-HG161		Met inhibitor.	Phase 1 (Solid Tumor)
	HS-10241		Met inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Merestinib		Multi-kinase inhibitor targeting Met, Ros1, Axl, Flt3, and other proteins.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Gallbladder carcinoma, Cholangiocarcinoma, Lung cancer)
	Ningetinib		Multi-kinase inhibitor targeting Axl, Met, VEGFR-2, and Flt3.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Renal cell carcinoma)
	OMO-1		Met inhibitor.	Phase 2 (Solid Tumor)
	REGN5093		anti-Met bispecific antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	REGN5093-M114		Anti-Met bispecific antibody drug conjugate.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	RXDX-106		Met and TAM (Tyro3, Axl, Mer) inhibitor.	Phase 1 (Solid Tumor)
	SAR125844		Met inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	Savolitinib		Met inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Renal cell carcinoma, Lung cancer)
	SHR-A1403		anti-Met antibody-drug conjugate.	Phase 1 (Solid Tumor)
	Sitravatinib		Multi-kinase inhibitor.	Phase 3 (Lung adenocarcinoma) Phase 2 (Non-small cell lung carcinoma (NSCLC), Renal cell carcinoma, Urothelial carcinoma, Liposarcoma)
	Sym015		Anti-Met antibody mixture.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Solid Tumor)
	TAS-115		A multi-kinase inhibitor (VEGFR, MET, and CSF1R).	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Alveolar soft part sarcoma)
	Telisotuzumab vedotin		Anti-Met antibody drug conjugate.	Phase 1 (Solid Tumor)
	Tepotinib	Tepmetko	Met inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (NSCLC with a MET exon 14 skipping mutation)
	unecritinib		Alk/Met/Ros1 kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Solid Tumor, Anaplastic large cell lymphoma (ALCL))
	XL092		Multi-kinase inhibitor.	Phase 1 (Solid Tumor)
EGFR L858R	ABT-101		Egfr/Her2 inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Head and neck squamous cell carcinoma (HNSCC))
	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))
	AZD3759		Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	BBT-176		Fourth generation Egfr inhibitor targeting exon 19del/L858R, T790M, and C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	BDTX-1535		Irreversible brain-penetrant fourth generation Egfr inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Glioma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Befotertinib		Third generation mutation-specific (T790M, L858R, exon 19 deletion) Egfr tyrosine kinase inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC))
	BLU-451		Egfr inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	BLU-701		Fourth generation Egfr inhibitor targeting exon 19del, L858R, and C797X resistance mutations.	Phase 2 (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))
	BPI-7711		Egfr T790M inhibitor.	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)
	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		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)
	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))

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	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		Third generation mutation-specific Egfr tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	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)
	Naquotinib		EGFR mutant-specific inhibitor.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	Nazartinib		Third generation EGFR mutant-specific (T790M, L858R, exon 19 deletion) tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	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)
	Olmutinib		Egfr inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	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)
	PF-06747775		Egfr T790M-specific inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC))
	TAS3351		Fourth generation Egfr inhibitor targeting T790M and T790M /C797S mutations.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	ZN-e4		Egfr T790M inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC))
EGFR Amplification	ABBV-221		Anti-Egfr antibody drug conjugate.	Phase 1 (Solid Tumor)
	ABBV-321		Anti-Egfr antibody conjugated to monomethyl auristatin F.	Phase 1 (Solid Tumor) Phase 1 (Glioblastoma, Head and neck squamous cell carcinoma (HNSCC), Brain and Central Nervous System Tumors, Lung squamous cell carcinoma)
	ABT806		Anti-Egfr and EGFRvIII antibody.	Phase 1 (Solid Tumor) Phase 2 (Gastroesophageal junction carcinoma)
	ASP-1929		An antibody-dye conjugate comprised of cetuximab and IRDye700DX acting as photoimmunotherapy.	Phase 3 (Head and neck carcinoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	AVID100		Anti-Egfr antibody-drug conjugate with DM1.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Breast carcinoma (triple negative))
	AZD9592		Bispecific anti-Met/Egfr antibody drug conjugate.	Phase 1 (Solid Tumor)
	BCA101		Anti-Egfr antibody fused to the extracellular domain of human TGF-beta receptor II.	Phase 1 (Solid Tumor) Phase 1 (Head and neck squamous cell carcinoma (HNSCC), Brain and Central Nervous System Tumors, Anal squamous cell carcinoma)
	CMAB009		Anti-Egfr monoclonal antibody.	Phase 3 (Colorectal carcinoma (CRC))
	CPGJ602		Recombinant human-mouse chimeric anti-Egfr monoclonal antibody.	Phase 2 (Colorectal carcinoma (CRC))
	D2C7-IT		Immunotoxin targeting both wild-type Egfr and Egfr-vIII.	Phase 1 (Glioblastoma)
	EGFR(V)-EDV-Dox		Doxorubicin-loaded EGFR-targeting nanocells.	Phase 1 (Glioblastoma)
	GC1118		Anti-Egfr monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Glioblastoma, Gastroesophageal junction carcinoma)
	KL-140		Anti-Egfr monoclonal antibody.	Phase 3 (Colorectal carcinoma (CRC))
	MM-151		Anti-Egfr monoclonal antibody mixture.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor)
	Nimotuzumab	Theraloc	Anti-Egfr monoclonal antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Gastric carcinoma, Glioblastoma, Glioma, Pancreatic carcinoma, Head and neck carcinoma, Gastroesophageal junction carcinoma, Esophageal carcinoma, Cervical carcinoma)
	REGN7075		anti-EGFR/CD28 bispecific antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Cutaneous squamous cell carcinoma, Breast carcinoma (triple negative), Colorectal carcinoma (CRC))
	SI-B001		Anti-Egfr/ErbB3 bispecific antibody.	Phase 3 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Esophageal carcinoma)
	Sym004		Anti-Egfr antibody mixture.	Phase 2 (Glioma, Head and neck squamous cell carcinoma (HNSCC), Colorectal carcinoma (CRC))
	SYN004		Anti-Egfr monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Lung squamous cell carcinoma)
	TAK-186		A Conditional Bispecific Redirected Activation (COBRA) Protein targeting Egfr and CD3.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Colorectal carcinoma (CRC))
EGFR Amplification L858R	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

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				EGFR exon 20 insertion)
	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-189		Irreversible Egfr/Her2 inhibitor.	Phase 2 (Solid Tumor)
	BL-B01D1		an EGFR x ERBB3 bispecific antibody-drug conjugate.	Phase 1 (Non-small cell lung carcinoma (NSCLC))
	ERAS-601		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))
	HBI-2376		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	Lifirafenib		Dual Braf/Egfr inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Solid Tumor, Brain and Central Nervous System Tumors)
	Modotuximab		Anti-EGFR antibody.	Phase 1 (Gastric carcinoma, Colorectal carcinoma (CRC))
	Neratinib	Nerlynx	Egfr/Her2/ErbB4 inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Breast carcinoma (HER2+))
	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)
	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)
	Varlitinib		Egfr/Her2 kinase inhibitor.	Phase 2 (Gastric carcinoma, Hepatocellular carcinoma (HCC), Pancreatic carcinoma, Cholangiocarcinoma)
	WSD0922-FU		Blood-brain barrier penetrable EGFR/EGFRvIII inhibitor.	Phase 1 (Non-small cell lung carcinoma (NSCLC)) Phase 1 (Glioblastoma, Anaplastic astrocytoma)
TP53 P278H R110fs	Adavosertib		Wee1 tyrosine kinase inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 2 (Lymphoma, Embryonal tumor with multi-layered rosettes (ETMR), Medulloblastoma, Small cell lung carcinoma (SCLC), Solid Tumor, Primary myelofibrosis (PMF), Ovarian carcinosarcoma, Acute myeloid leukemia (AML), MDS/MPN, unclassifiable, Chronic myelomonocytic leukemia (CMML), Peritoneal papillary serous carcinoma, Myelodysplastic Syndrome (MDS))
	AL8326		Aurora kinase B/VEGFRs/Fgfr multi-kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Small cell lung carcinoma (SCLC))

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Alisertib		Aurora kinase A inhibitor.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) Phase 3 (Peripheral T-cell lymphoma (PTCL))
	AMG 900		Aurora kinase A/B/C inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Acute myeloid leukemia (AML))
	AT9283		Aurora kinase A/B, Jak2, Jak3, Bcr-Abl inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Acute myeloid leukemia (AML), Multiple myeloma (MM), Acute lymphoblastic leukemia (ALL))
	ATO	Trisenox	PML-RARA inhibitor. Inhibits multiple signaling pathways, including the Hedgehog pathway.	Phase 2 (Non-small cell lung carcinoma (NSCLC)) FDA Approved in other indications (Acute myeloid leukemia (AML), Acute promyelocytic leukemia (APL))
	AZD2811		Nanoparticle formulation of Aurora kinase B inhibitor barasertib (AZD1152).	Phase 1 (Solid Tumor) Phase 2 (Acute myeloid leukemia (AML), Myelodysplastic Syndrome (MDS))
	Debio 0123		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor)
	ENMD-2076		Aurora kinase A inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Fibrolamellar hepatocellular carcinoma, Ovarian carcinoma, Breast carcinoma, Fallopian tube adenocarcinoma, Sarcoma)
	EP0042		Aurora kinase A/B and Flt3 inhibitor.	Phase 2 (Acute myeloid leukemia (AML), Chronic myelomonocytic leukemia (CMML), Myelodysplastic Syndrome (MDS))
	IMP7068		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor)
	JAB-2485		Aurora kinase A inhibitor.	Phase 2 (Solid Tumor)
	Kevetrin		Blocks Mdm2-p53 interaction, restoring transcriptional activity of p53.	Phase 1 (Solid Tumor) Phase 2 (Ovarian carcinoma)
	LY3295668		Aurora kinase A inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Small cell lung carcinoma (SCLC), Breast carcinoma (triple negative), Breast carcinoma (hormone receptor +, HER2-))
	SGT-53		TP53 gene therapy delivered via transferrin-targeted nanoparticles.	Phase 1 (Solid Tumor) Phase 2 (Glioblastoma, Glioma, Pancreatic carcinoma)
	SNS-314		Aurora kinase A/B inhibitor.	Phase 1 (Solid Tumor)
	SY-4835		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor)
	TAS-119		Aurora kinase A inhibitor.	Phase 1 (Solid Tumor)
	TT-00420		Aurora kinase A/B inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Breast carcinoma (triple negative))
TP53 P278H	COTI-2		Reactivates mutant p53.	Phase 1 (Endometrial carcinoma, Head and neck squamous cell carcinoma (HNSCC), Ovarian carcinoma, Cervical carcinoma)

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
EGFR L858R	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 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. [2,5-11]. Afatinib has additionally been FDA-approved for the treatment of NSCLC with S768I, L861Q, and/or G719X mutations. [12]. The combination of erlotinib and ramucirumab has been FDA-approved for the treatment of metastatic NSCLC patients with tumors harboring an EGFR exon 19 deletion or the exon 21 L858R mutation. [13]. Amivantamab has been approved by the FDA for NSCLC patients with EGFR exon 20 insertions, whose disease has progressed on or after platinum-based chemotherapy. 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. [14-17]. 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. [2,5-7,11,13,18]. Less common activating EGFR mutations have variable sensitivity to EGFR tyrosine kinase inhibitors. [19]. However, activation of Met, through MET amplification or high Met protein expression, has been implicated in resistance to Egfr tyrosine kinase inhibitors. [20-22].	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. [20,23-26]. 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. [27-31]. 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. [32-35]. Preclinical studies have reported increased Smo expression in NSCLC cell lines resistant to first, second, and third generation Egfr inhibitors as compared with sensitive ones; treatment with Smo inhibitors was observed to restore sensitivity in the resistant cell lines. [36-38].
MET Amplification	Met protein activation or overexpression promotes angiogenesis, resistance to apoptosis, proliferation, and invasion of cancer cells. [39-42]. Activation of Met, resulting from either MET mutation or	Increased Met expression, possibly as a result of MET mutation or amplification, may lead to enhanced Met activation and may therefore confer sensitivity to Met inhibitors. [47,48]. Crizotinib and cabozantinib	MET amplification or elevated Met expression has been implicated in acquired resistance to Egfr inhibitors in some cancer types; studies are currently investigating combination therapy with Met inhibitors and Egfr

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
	amplification, has been reported to promote cell growth and tumorigenesis in preclinical NSCLC models. [43-45]. Met protein expression in NSCLC has been associated with a predisposition to the development of brain metastases. [22,46].	target multiple kinases, including Met, and have been approved for certain indications. [49-56]. In addition, the kinase inhibitors capmatinib and tepotinib have been approved by the FDA, EMA and PMDA, for the treatment of adult patients with metastatic non-small cell lung cancer and a MET exon 14 skipping mutation. [57,58]. NSCLC patients harboring MET exon 14 skipping alterations or MET amplification have been reported to respond to crizotinib. [59-62].	inhibitors in this setting. [20,63-65]. Met activation has been implicated as one key mechanism of resistance to Egfr-targeted therapy in NSCLC. [20-22,66-68] .
TP53 P278H	Loss of tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers. [69]. 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. [70-72]. Expression of p53 in normal 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. [73-77]. TP53 alterations are believed to be early events in NSCLC, preceding lymph node metastasis. [78]. 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. [79-82]. TP53 mutation has been associated with PD-L1 expression and T-cell infiltration in lung adenocarcinoma samples. [83-87]. TP53 mutations have been significantly associated with the development of distant metastases after diagnosis in early-stage NSCLC in a cohort of 759 patients. [88].	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. [89-91]. Inhibition of components of the DNA damage checkpoint, including Wee1, has been reported to enhance the activity of DNA-damaging agents in preclinical cancer models with deficiency of p53 function. [92-94]. 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. [95-100].	Mutations in TP53 may increase resistance to ionizing radiation therapy. [101,102].
TP53 R110fs	Loss of tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers. [69]. 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.	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. [89-91]. Inhibition of components of the DNA damage checkpoint, including Wee1, has been	Mutations in TP53 may increase resistance to ionizing radiation therapy. [101,102].

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
	[70-72]. Expression of p53 in normal 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. [73-77]. TP53 alterations are believed to be early events in NSCLC, preceding lymph node metastasis. [78]. 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. [79-82]. TP53 mutation has been associated with PD-L1 expression and T-cell infiltration in lung adenocarcinoma samples. [83-87]. TP53 mutations have been significantly associated with the development of distant metastases after diagnosis in early-stage NSCLC in a cohort of 759 patients. [88].	reported to enhance the activity of DNA-damaging agents in preclinical cancer models with deficiency of p53 function. [92-94]. 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. [95-100].	
EGFR Amplification	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].	EGFR amplification or increased copy number may result in elevated Egfr protein expression and thus predict sensitivity to Egfr targeted therapies. The Egfr tyrosine kinase inhibitors (TKIs) erlotinib, afatinib, gefitinib, osimertinib, and dacomitinib have been approved for the treatment of non-small cell lung carcinoma (NSCLC) with specific EGFR mutations; however, only modest clinical benefit for gefitinib or erlotinib has been reported in patients harboring EGFR amplification without concurrent sensitizing mutations. [6,8,12,103-107]. Anti-Egfr monoclonal antibodies are also approved in some indications, including cetuximab, which is an approved therapy for head and neck and colorectal cancer, and panitumumab, which is approved in colorectal cancer. [108-110]. However, molecular analyses of tumor samples from a Phase 3 study in head and neck squamous cell carcinoma revealed that neither Egfr expression nor EGFR amplification predicted response to cetuximab. [111,112]. 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,	EGFR amplification has been reported as an acquired alteration in 15.5% (16 /103) of EGFR exon19del or L858R-mutant NSCLC patients who were treated with Egfr TKI and in 9.7% (3 /31) of patients treated with Egfr TKI in combination with bevacizumab. [113].

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
		afatinib, gefitinib, dacomitinib, and the combination of erlotinib plus ramucirumab. [2,5-7,11,13,18]. Less common activating EGFR mutations have variable sensitivity to EGFR tyrosine kinase inhibitors. [19].	

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