Taipei Veterans General Hospital

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Sample Information

Patient Name: 黃紫珍
Gender: Female
ID No.: N220231103
History No.: 30689339
Age: 53

Ordering Doctor: DOC3014F 陳育民
Ordering REQ.: C2193HK
Signing in Date: 2020/07/23

Path No.: S109-99747
MP No.: F20045
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-19776A
Percentage of tumor cells: 20%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

3 Relevant Biomarkers
16 Therapies Available
199 Clinical Trials

Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	***EGFR p.(L858R) c.2573T>G***	NTRK3	Not detected
ERBB2	Not detected	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	***MET amplification***		

Relevant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
EGFR p.(L858R) c.2573T>G epidermal growth factor receptor Tier: IA Allele Frequency: 14.19%	**afatinib** [1, 2] **dacomitinib** [1, 2] **erlotinib** [1, 2] **gefitinib** [1, 2] **osimertinib** [1, 2] **bevacizumab* + erlotinib** [2] **erlotinib + ramucirumab** [2] afatinib + cetuximab atezolizumab + bevacizumab + chemotherapy gefitinib + chemotherapy bevacizumab + gefitinib	None	187
MET amplification MET proto-oncogene, receptor tyrosine kinase Tier: IA	crizotinib	None	18
AR amplification androgen receptor Tier: IIC	None	androgen receptor therapy bicalutamide leuprorelin	0

Public data sources included in relevant therapies: FDA1, NCCN, **EMA**2, ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.
*** Includes biosimilars**

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	14.19%	NM_005228.4	missense	1995
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	99.95%	NM_004304.4	missense	1998
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	100.00%	NM_004304.4	missense	1996
ALK	p.(=)	c.3375C>A	.	chr2:29445458	100.00%	NM_004304.4	synonymous	1993
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.86%	NM_000142.4	synonymous	1379
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.95%	NM_006206.5	synonymous	1996
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	98.92%	NM_213647.2	missense	1481
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.90%	NM_020975.4	synonymous	1991

Variant Details (continued)

Copy Number Variations

Gene	Locus	Copy Number
MET	chr7:116313480	7.4
AR	chrX:66776186	6.45

Biomarker Descriptions

AR (androgen receptor)

Background: The AR gene encodes the androgen receptor protein (AR), a ligand-activated transcription factor regulated by the binding of the hormones testosterone and dihydrotestosterone[1,2]. Hormone binding to AR results in receptor dimerization, nuclear translocation, and target gene transcription, thus activating the RAS/RAF/MEK/ERK and PI3K/AKT/MTOR signaling pathways, which promote cell proliferation and survival[2,3,4].

Alterations and prevalence: Alterations in AR function can result from overexpression, gene amplification, or mutations. AR mutations, including L702H, W742C/L, H875Y, and T878A, are commonly observed in 10-30% of castration-resistant prostate cancer and result in decreased ligand specificity, allowing other nuclear hormones to activate AR[5]. Androgen receptor splice variants have been reported in castration resistant prostate cancer[6,7]. The androgen receptor splice variant 7 (AR-V7) is a result of aberrant mRNA splicing of AR exons 1-3 and a cryptic exon 3, resulting in the expression of a constitutively active protein[7].

Potential relevance: The FDA has granted fast track designation (2016) to seviteronel for AR-positive triple-negative breast cancer (TNBC) patients[8]. Androgen deprivation therapy (ADT) such as abiraterone[9] (2011) and enzalutamide[10] (2011) are FDA approved for use in locally advanced and metastatic prostate cancers. Although many men initially respond to ADT, most will develop hormone resistance. Resistance to ADT is also associated with other aberrations of the AR gene including mutations within the ligand binding domain and gene amplification[5,11,12]. The androgen receptor splice variant, AR-V7, lacks the ligand binding domain, resulting in constitutive activation and is associated with resistance to androgen deprivation therapy (ADT) in advanced prostate cancer[6].

EGFR (epidermal growth factor receptor)

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the human epidermal growth factor receptor (HER) family. Along with EGFR/ERBB1/HER1, ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family[13]. EGFR ligand induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling pathways including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways. Activation of these pathways promote cell proliferation, differentiation, and survival[14,15].

Alterations and prevalence: Recurrent somatic mutations in the tyrosine kinase domain of EGFR are observed in approximately 10-20% of lung adenocarcinoma and at higher frequencies in never-smoker, female, and in Asian populations with lung cancer[16,17,18,19]. The most common mutations occur near the ATP-binding pocket of the kinase domain and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 21[20]. These mutations constitutively activate the EGFR kinase resulting in downstream signaling and represent 80% of the EGFR mutations observed in lung cancer. A second group of recurrent activating mutations that are less common include E709K, G719X, S768I, L861Q, and short in-frame insertions in exon 20[21,22,23,24]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[25]. Although these variants are common in lung cancer, they are rare in other cancer types. In glioblastoma, recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V[20,26]. The recurrent focal amplification of the EGFR gene leads to an increase in expression in several cancer types. EGFR is amplified in up to 30% of glioblastoma, 12% of esophageal cancer, 10% of head and neck cancer, 5% of bladder cancer, and 5% of lung squamous cell carcinoma[17,18,19,26,27]. Deletion of exons 2-7 encoding the extracellular domain of EGFR (EGFRvIII) results in overexpression of a ligand-independent constitutively active protein which is frequently observed in glioblastoma and has been shown to lead to lung cancer development as well as sensitivity to TKIs[28,29,30].

Potential relevance: Erlotinib[31] (2004), afatinib[32] (2013), gefitinib[33] (2015), osimertinib[34] (2015), and dacomitinib[35] (2018) are small molecule TKIs that are FDA approved for non-small cell lung cancer (NSCLC) patients with sensitizing exon 19 deletions and exon

Biomarker Descriptions (continued)

21 L858R mutations. Acquired secondary mutations often confer resistance to first line TKI therapy with the T790M amino acid substitution accounting for 50-60% of cases[20]. Osimertinib is also indicated for NSCLC patients harboring EGFR T790M mutations whose disease has progressed on or after treatment with a first line TKI. EGFR targeting antibodies including cetuximab[36] (2004), panitumumab[37] (2006), and necitumumab[38] (2016) are also under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The use of cetuximab in combination with afatinib is currently recommended by the NCCN for patients who have progressed after receiving erlotinib, afatinib, dacomitinib, or gefitinib and chemotherapy[39].

MET (MET proto-oncogene, receptor tyrosine kinase)

Background: The MET proto-oncogene encodes a receptor tyrosine kinase for the hepatocyte growth factor (HGF) protein, which is expressed by mesenchymal cells. Ubiquitin-dependent proteolysis regulates the steady state level of the MET protein via recognition of the tyrosine phosphorylation site Y1003 in the MET Cbl-binding domain within the juxtamembrane region[40,41,42]. Growth factor signaling leads to MET dimerization and subsequent initiation of downstream effectors including those involved in the RAS/RAF/MEK/ERK and PI3K/AKT signaling pathways, which regulate cell migration, proliferation, and survival[43,44].

Alterations and prevalence: Recurrent somatic MET alterations include activating mutations, gene amplification, and translocations generating MET gene fusions. Recurrent somatic mutations fall into two classes, mutations in the MET kinase domain, which are uncommon, and splice-site mutations affecting exon 14. Recurrent kinase domain mutations are observed in papillary renal cell carcinoma (PRCC) (1-2%) and include M1250T, H1094Y, and V1070E. Mutation of the Y1003 phosphorylation site is reported in lung cancer but is uncommon (<1%)[19,26]. In contrast, splice-site mutations flanking exon 14 are observed in 4% of non-small cell lung cancer (NSCLC). These mutations include canonical splice site mutations affecting exon 14 and deletions that extend into the splicing motifs within intron 13[45,46]. Such mutations disrupt splicing leading to the formation of an alternative transcript that joins exon 13 directly to exon 15 and skips exon 14 entirely. The MET exon 14 skipping transcript lacks the juxtamembrane domain that contains the recognition motif for ubiquitin-dependent proteolysis and thus leads to a marked increase in steady-state level of the MET protein[47]. MET exon 14 skipping mutations act as oncogenic drivers in lung cancer mutually exclusive to activating mutations in EGFR and KRAS and other oncogenic fusions such as ALK and ROS1[45,48,49]. MET is amplified in 2-5% of ovarian cancer, esophageal adenocarcinoma, stomach adenocarcinoma, glioblastoma, and lung adenocarcinoma[19,26,50]. Recurrent MET fusions, although infrequent, are observed in adult and pediatric glioblastoma, papillary renal cell carcinoma, lung cancer, liver cancer, thyroid cancer, and melanoma[51,52,53]. MET alterations are believed to be enriched in late-stage cancers where they drive tumor progression and metastasis[54,55,56].

Potential relevance: The FDA has granted designations for two investigational MET inhibitors— capmatinib[57] has been granted FDA orphan drug and breakthrough therapy designations for MET exon 14 skipping positive metastatic NSCLC following platinum-based chemotherapy, and tepotinib[58] has been granted FDA breakthrough designation (2019) for advanced MET exon 14 skipping NSCLC. MET exon 14 skipping mutations confer sensitivity to approved kinase inhibitors including crizotinib (2011), which is recommended for MET amplifications and exon 14 skipping mutations[39,45,48,49]. Conversely, amplification of MET has been observed to mediate resistance to EGFR tyrosine kinase inhibitors (TKIs)[59,60,61,62,63]. In a phase II trial testing the MET inhibitor savolitinib, patients with advanced PRCC exhibited median progression free survival (PFS) of 6.2 and 1.4 months for MET-driven and MET-independent PRCC, respectively[64].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	●	●	●	●	● (IV)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
gefitinib	●	●	●	●	● (IV)
erlotinib	●	●	●	●	● (III)
osimertinib	●	●	●	●	● (III)
dacomitinib	●	●	●	●	✖
bevacizumab + erlotinib	✖	●	●	●	● (II)
erlotinib + ramucirumab	✖	●	●	●	✖
afatinib + cetuximab	✖	●	✖	✖	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
bevacizumab + gefitinib	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
anlotinib hydrochloride, toripalimab	✖	✖	✖	✖	● (IV)
apatinib + EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
apatinib + gefitinib	✖	✖	✖	✖	● (IV)
bevacizumab + osimertinib, osimertinib	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
erlotinib, gefitinib, icotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (IV)
gefitinib, radiation therapy	✖	✖	✖	✖	● (IV)
icotinib hydrochloride	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, icotinib hydrochloride + chemotherapy	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, radiation therapy	✖	✖	✖	✖	● (IV)
ASK120067, gefitinib	✖	✖	✖	✖	● (III)
bevacizumab (Shanghai Hengrui Pharmaceutical) + chemotherapy, bevacizumab + chemotherapy	✖	✖	✖	✖	● (III)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab, atezolizumab, chemotherapy	✖	✖	✖	✖	● (III)
bevacizumab, erlotinib	✖	✖	✖	✖	● (III)
BPI-7711, gefitinib	✖	✖	✖	✖	● (III)
durvalumab, chemotherapy	✖	✖	✖	✖	● (III)
erlotinib, chemotherapy	✖	✖	✖	✖	● (III)
erlotinib, erlotinib + chemotherapy	✖	✖	✖	✖	● (III)
gefitinib + chemotherapy	✖	✖	✖	✖	● (III)
gefitinib, anlotinib hydrochloride	✖	✖	✖	✖	● (III)
gefitinib, apatinib	✖	✖	✖	✖	● (III)
gefitinib, chemotherapy	✖	✖	✖	✖	● (III)
gefitinib, erlotinib	✖	✖	✖	✖	● (III)
gefitinib, erlotinib, gefitinib + radiation therapy, erlotinib + radiation therapy	✖	✖	✖	✖	● (III)
gefitinib, icotinib hydrochloride, erlotinib, gefitinib + radiation therapy, icotinib hydrochloride + radiation therapy, erlotinib + radiation therapy	✖	✖	✖	✖	● (III)
HS-10296, gefitinib	✖	✖	✖	✖	● (III)
icotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (III)
icotinib hydrochloride, icotinib hydrochloride + radiation therapy	✖	✖	✖	✖	● (III)
nivolumab, chemotherapy	✖	✖	✖	✖	● (III)
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
pembrolizumab, chemotherapy	✖	✖	✖	✖	● (III)
AZD-3759, erlotinib, gefitinib	✖	✖	✖	✖	● (II/III)
afatinib + DFP-14323, erlotinib + DFP-14323, osimertinib + DFP-14323	✖	✖	✖	✖	● (II)
afatinib, bevacizumab	✖	✖	✖	✖	● (II)

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Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib, chemotherapy, radiation therapy	✖	✖	✖	✖	● (II)
anlotinib hydrochloride + icotinib hydrochloride	✖	✖	✖	✖	● (II)
anlotinib hydrochloride, erlotinib, icotinib hydrochloride, gefitinib	✖	✖	✖	✖	● (II)
atezolizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab + gefitinib + chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, erlotinib, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, osimertinib	✖	✖	✖	✖	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✖	✖	✖	✖	● (II)
chemotherapy, atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)
chemotherapy, ramucirumab	✖	✖	✖	✖	● (II)
crizotinib + chemotherapy	✖	✖	✖	✖	● (II)
durvalumab, tremelimumab, chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✖	✖	✖	✖	● (II)
erlotinib + chemotherapy	✖	✖	✖	✖	● (II)
erlotinib + surgical intervention	✖	✖	✖	✖	● (II)
erlotinib, bevacizumab + erlotinib	✖	✖	✖	✖	● (II)
erlotinib, gefitinib	✖	✖	✖	✖	● (II)
erlotinib, radiation therapy	✖	✖	✖	✖	● (II)
famitinib, HS-10296	✖	✖	✖	✖	● (II)
gefitinib + fulvestrant	✖	✖	✖	✖	● (II)
gefitinib + nazartinib	✖	✖	✖	✖	● (II)
gefitinib, surgical intervention	✖	✖	✖	✖	● (II)

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Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
gefitinib, thalidomide	✖	✖	✖	✖	● (II)
icotinib hydrochloride + radiation therapy	✖	✖	✖	✖	● (II)
icotinib hydrochloride + radiation therapy, icotinib hydrochloride	✖	✖	✖	✖	● (II)
nivolumab, ipilimumab	✖	✖	✖	✖	● (II)
osimertinib + radiation therapy	✖	✖	✖	✖	● (II)
osimertinib + selumetinib	✖	✖	✖	✖	● (II)
osimertinib, afatinib	✖	✖	✖	✖	● (II)
osimertinib, bevacizumab	✖	✖	✖	✖	● (II)
osimertinib, gefitinib + osimertinib	✖	✖	✖	✖	● (II)
osimertinib, radiation therapy	✖	✖	✖	✖	● (II)
osimertinib, ramucirumab	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
pembrolizumab + chemotherapy	✖	✖	✖	✖	● (II)
poziotinib	✖	✖	✖	✖	● (II)
ramucirumab, osimertinib	✖	✖	✖	✖	● (II)
tepotinib, osimertinib	✖	✖	✖	✖	● (II)
tyrosine kinase inhibitors, radiation therapy	✖	✖	✖	✖	● (II)
zoledronic acid, gefitinib	✖	✖	✖	✖	● (II)
AZD-3759	✖	✖	✖	✖	● (I/II)
bevacizumab + erlotinib + chemotherapy	✖	✖	✖	✖	● (I/II)
CBT-502, anlotinib hydrochloride	✖	✖	✖	✖	● (I/II)
DZD-9008	✖	✖	✖	✖	● (I/II)
EMB01	✖	✖	✖	✖	● (I/II)
erlotinib + trametinib	✖	✖	✖	✖	● (I/II)
gefitinib + osimertinib	✖	✖	✖	✖	● (I/II)

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Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
icotinib hydrochloride + chemotherapy + radiation therapy	✖	✖	✖	✖	● (I/II)
KP-673	✖	✖	✖	✖	● (I/II)
lazertinib	✖	✖	✖	✖	● (I/II)
ningetinib, gefitinib	✖	✖	✖	✖	● (I/II)
oleclumab + osimertinib	✖	✖	✖	✖	● (I/II)
S-49076, gefitinib	✖	✖	✖	✖	● (I/II)
telaglenastat, osimertinib	✖	✖	✖	✖	● (I/II)
U3-1402	✖	✖	✖	✖	● (I/II)
afatinib, chemotherapy	✖	✖	✖	✖	● (I)
afatinib, immunostimulant	✖	✖	✖	✖	● (I)
afatinib, osimertinib	✖	✖	✖	✖	● (I)
alisertib, osimertinib	✖	✖	✖	✖	● (I)
anlotinib hydrochloride + erlotinib	✖	✖	✖	✖	● (I)
CK-101	✖	✖	✖	✖	● (I)
dacomitinib, osimertinib	✖	✖	✖	✖	● (I)
DS-1205c, gefitinib	✖	✖	✖	✖	● (I)
DS-1205c, osimertinib	✖	✖	✖	✖	● (I)
EGFR tyrosine kinase inhibitor, anlotinib hydrochloride	✖	✖	✖	✖	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)
genolimzumab, fruquintinib	✖	✖	✖	✖	● (I)
JNJ-61186372	✖	✖	✖	✖	● (I)
lazertinib, JNJ-61186372	✖	✖	✖	✖	● (I)
nazartinib + trametinib, nazartinib + ribociclib, LXH254 + nazartinib, capmatinib + nazartinib, gefitinib + nazartinib	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
niraparib, osimertinib	✖	✖	✖	✖	● (I)
nivolumab, ipilimumab, radiation therapy	✖	✖	✖	✖	● (I)
osimertinib + radiation therapy, osimertinib	✖	✖	✖	✖	● (I)
osimertinib, necitumumab	✖	✖	✖	✖	● (I)
osimertinib, sapanisertib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
SH-1028	✖	✖	✖	✖	● (I)
telisotuzumab vedotin, osimertinib	✖	✖	✖	✖	● (I)
TNO-155	✖	✖	✖	✖	● (I)
TP-0903	✖	✖	✖	✖	● (I)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	✖	✖	✖	✖	● (I)

MET amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
crizotinib	✖	●	✖	✖	● (II)
cabozantinib	✖	✖	✖	✖	● (II)
capmatinib	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
telisotuzumab vedotin	✖	✖	✖	✖	● (II)
tepotinib, osimertinib	✖	✖	✖	✖	● (II)
OMO-1	✖	✖	✖	✖	● (I/II)
REGN-5093	✖	✖	✖	✖	● (I/II)
S-49076, gefitinib	✖	✖	✖	✖	● (I/II)
glumetinib	✖	✖	✖	✖	● (I)
JNJ-61186372	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

MET amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
metatinib	✖	✖	✖	✖	● (I)
TPX-0022	✖	✖	✖	✖	● (I)

AR amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
androgen receptor therapy	✖	○	✖	✖	✖
bicalutamide	✖	○	✖	✖	✖
leuprorelin	✖	○	✖	✖	✖

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Details

Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

FDA information is current as of 2020-02-28. For the most up-to-date information, search www.fda.gov.

EGFR p.(L858R) c.2573T>G

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-10-11 **Variant class:** EGFR L858R mutation

Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

- First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of GILOTRIF® were not established in patients whose tumors have resistant EGFR mutations

- Treatment of patients with metastatic, squamous NSCLC progressing after platinum-based chemotherapy

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/201292s015lbl.pdf

EGFR p.(L858R) c.2573T>G (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-09-27 **Variant class:** EGFR L858R mutation

Indications and usage:
VIZIMPRO® is a kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211288s000lbl.pdf

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2016-10-18 **Variant class:** EGFR L858R mutation

Indications and usage:

TARCEVA® is a kinase inhibitor indicated for:

- The treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

Limitations of Use:

- Safety and efficacy of TARCEVA® have not been established in patients with NSCLC whose tumors have other EGFR mutations.
- TARCEVA® is not recommended for use in combination with platinum-based chemotherapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021743s025lbl.pdf

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-08-22 **Variant class:** EGFR L858R mutation

Indications and usage:

IRESSA® is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of IRESSA® have not been established in patients whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206995s003lbl.pdf

EGFR p.(L858R) c.2573T>G (continued)

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-12-19 **Variant class:** EGFR L858R mutation

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for

- the first-line treatment of patients with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208065s013lbl.pdf

Current NCCN Information

In this cancer type | In other cancer type | In this cancer type and other cancer types | Contraindicated | Not recommended | Resistance

NCCN information is current as of 2019-11-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

EGFR p.(L858R) c.2573T>G

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

EGFR p.(L858R) c.2573T>G (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Squamous Non-Small Cell Lung Cancer; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

EGFR p.(L858R) c.2573T>G (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

EGFR p.(L858R) c.2573T>G (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy) (Preferred)
- Progression on osimertinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Non-Squamous Non-Small Cell Lung Cancer; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Useful in Certain Circumstances)
- Non-Squamous Non-Small Cell Lung Cancer; Sensitizing EGFR mutation discovered during first-line systemic therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

EGFR p.(L858R) c.2573T>G (continued)

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Leptomeningeal and Spine metastases; Weekly pulse erlotinib (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

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afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

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afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

Other criteria: EGFR T790M negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Progression after receiving erlotinib, afatinib, dacomitinib, or gefitinib and systemic therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

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erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

EGFR p.(L858R) c.2573T>G (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Brain metastases; Newly diagnosed (Not specified)
- Non-Small Cell Lung Cancer; Leptomeningeal and Spine metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

alectinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

brigatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

EGFR p.(L858R) c.2573T>G (continued)

ceritinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

lorlatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

pembrolizumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

Other criteria: CD274 overexpression

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "A small study suggests that single-agent pembrolizumab is not effective as first-line therapy in patients with metastatic NSCLC and EGFR mutations, even those with PD-L1 levels more than 50%."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

MET amplification

● crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET amplification

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; High-level MET amplification; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

AR amplification

○ androgen receptor therapy

Cancer type: Head and Neck Cancer **Variant class:** AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent Metastatic Salivary Gland Tumors; Distant metastases; PS 0-3 (Therapy for recurrence)

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2019]

○ bicalutamide

Cancer type: Head and Neck Cancer **Variant class:** AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent Metastatic Salivary Gland Tumors; Distant metastases; PS 0-3 (Therapy for recurrence)

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2019]

○ leuprorelin

Cancer type: Head and Neck Cancer **Variant class:** AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent Metastatic Salivary Gland Tumors; Distant metastases; PS 0-3 (Therapy for recurrence)

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2019]

Current EMA Information

In this cancer type | In other cancer type | In this cancer type and other cancer types | Contraindicated | Not recommended | Resistance

EMA information is current as of 2020-02-28. For the most up-to-date information, search www.ema.europa.eu/ema.

EGFR p.(L858R) c.2573T>G

afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-02-13 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information_en.pdf

bevacizumab (Allergan) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-11-12 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/mvasi-epar-product-information_en.pdf

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-02-20 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/avastin-epar-product-information_en.pdf

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-06-05 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/vizimpro-epar-product-information_en.pdf

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-04-24 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/documents/product-information/tarceva-epar-product-information_en.pdf

EGFR p.(L858R) c.2573T>G (continued)

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-02-25 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/cyramza-epar-product-information_en.pdf

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-05-28 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information_en.pdf

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-02-25 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/tagrisso-epar-product-information_en.pdf

Current ESMO Information

In this cancer type | In other cancer type | In this cancer type and other cancer types | Contraindicated | Not recommended | Resistance

ESMO information is current as of 2019-11-01. For the most up-to-date information, search www.esmo.org.

EGFR p.(L858R) c.2573T>G

atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):
- Metastatic Non-Squamous; Magnitude of Clinical Benefit Scale Score version 1.1 score: 3 (First-line therapy)
- Metastatic ; PS 0-1; Without contraindications to immunotherapy after targeted therapies have been exploited (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

EGFR p.(L858R) c.2573T>G (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced stage; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):
- Stage IV; Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):
- Non-Squamous (Maintenance therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

EGFR p.(L858R) c.2573T>G (continued)

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):
- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

EGFR p.(L858R) c.2573T>G (continued)

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

bevacizumab + gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):
- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

EGFR p.(L858R) c.2573T>G (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):
- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):
- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):
- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

Signatures

Testing Personnel:

Shin-Ying Lin 2020.07.24 08:12:54 +08'00'

Laboratory Supervisor:

2020.07.24 08:13:10 +08'00'

Pathologist:

Yi-Chu Yeh 2020.07.24 08:13:23 +08'00'

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