

Key Clinical Biomarkers for Advanced NSCLC Management:

A Clinician's Resource

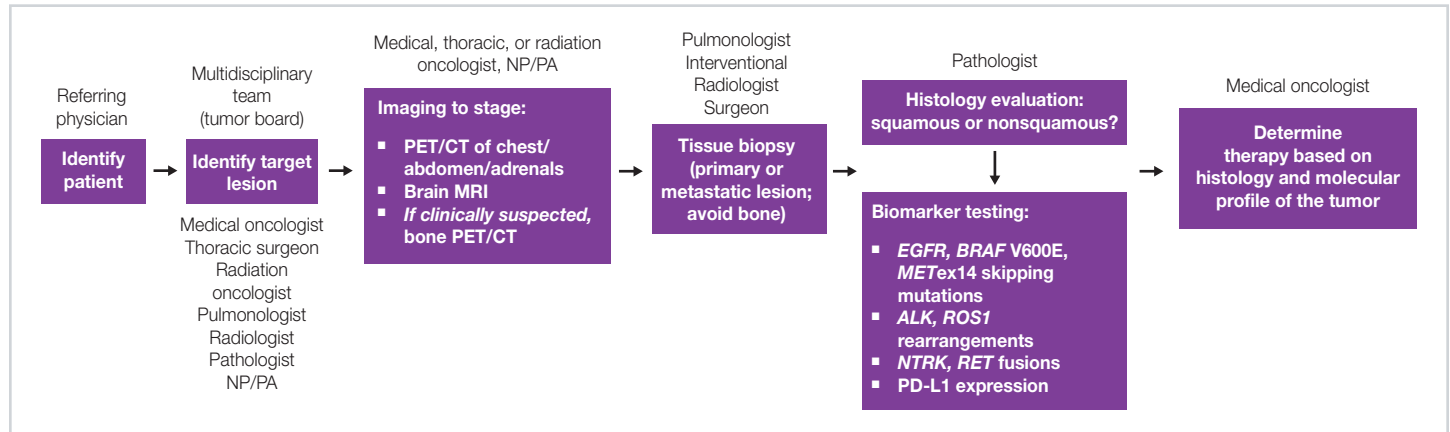


CLINICAL CARE OPTIONS®
ONCOLOGY

EVALUATION OF ADVANCED NSCLC

- Diagnosis of advanced NSCLC requires lesion assessment via x-ray, PET/CT imaging of chest/abdomen/pelvis, brain MRI, biopsy for pathologic assessment, and molecular testing (Figure 1)^[Gandara 2012]
- Histologic and biomarker assessment is key for guiding therapeutic selection and assists in predicting treatment response^[Lindeman 2018]

Figure 1. Diagnostic algorithm of advanced NSCLC.^[ESMO 2019; Pennell 2019; Lindeman 2018; Selpercatinib PI; Capmatinib PI]



Liquid Biopsy: Cell-Free DNA in Plasma^[Bernabé 2017]

- Useful option for biomarker testing, especially for the ~ 20% of patients who are not candidates for tissue biopsy (eg, insufficient availability of neoplastic tissue, lack of fitness of available tissue for biopsy, or biopsy is not technically feasible)
- *Limitation: false-negativity rate of ~ 30%; therefore, must retest using tumor tissue if results are negative*

BIOMARKER TESTING FOR NSCLC^[Masters 2015; ESMO 2019; Pennell 2019; Lindeman 2018]

- PD-L1 expression by IHC indicated in all histologic subtypes of NSCLC
- Testing for *EGFR*, *ALK*, *ROS1*, *BRAF* V600E, *NTRK*, *RET*, and *MET*ex14 is standard of care in nonsquamous NSCLC
- Broad NGS testing recommended and *preferred* to maximize number of mutations detected while minimizing tissue used^[Kalmekerian 2018; Pennell 2019]
 - For squamous NSCLC, experts recommend that broad NGS testing be considered or minimally testing same panel as for nonsquamous NSCLC in young patients (< 50 years), never/light smokers, Asian ethnicity, or if biopsy specimen small or shows mixed histology^[Lindeman 2018; Kalmekerian 2018; Hirsch 2018]
- All testing should be completed within 10-14 working days of biopsy^[Bernicker 2017; Pennell 2019]
 - **Wait for NGS results before acting on PD-L1 results**
 - Consider 1 cycle of chemotherapy for symptomatic patients while awaiting results
- Choice of assay for biomarker testing depends on institution, resources, and clinical context
 - Pathologists may use either cell blocks or other cytologic preparations as suitable specimens for lung cancer biomarker molecular testing^[Noll 2018; Dostader 2019]

Table 1. Comparison of Molecular Testing Approaches^[Hirsch 2018; Pennell 2018]

	Single Gene Testing	Multigene Testing (eg, by NGS)
Advantages	■ Potentially routine in practice ■ Potential for local implementation, rapid turnaround ■ Higher sensitivity with PCR platforms	■ Minimizes use of tumor tissue ■ Facilitates testing of multiple biomarkers, including emerging biomarkers for clinical trial enrollment ■ Need to know to test vs which biomarkers to test for ■ Generally less costly than sequential testing
Disadvantages	■ Tumor tissue samples often inadequate for multiple necessary tests ■ May lead to repeat biopsy procedures	■ Multiple platforms available using different methodology that affect types of alterations detected (eg, amplicon-based NGS does not detect gene fusions/rearrangements) ■ Analysis of complex biomarker reports ■ Preauthorization requirements ■ May not be easily accessible in community practice

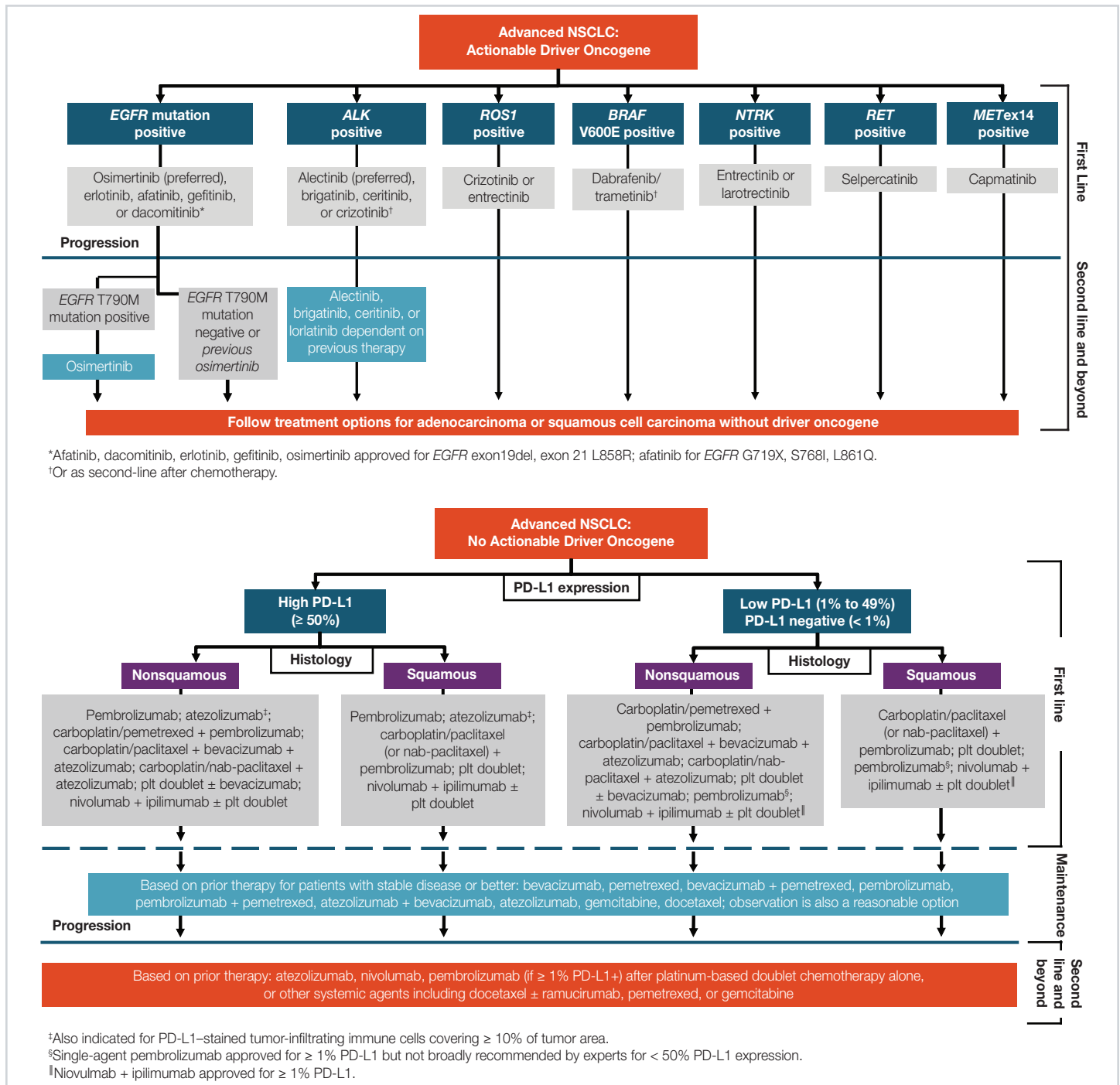
To download an expert-authored slideset with more detail on evolving biomarkers for precision therapy in lung cancer, please go to:

www.clinicaloptions.com/Lung2020Slides

TREATMENT OF ADVANCED NSCLC

- Mutational status, PD-L1 expression level, histology, patient age, performance status, and any existing comorbidities should be considered when selecting first-line and subsequent treatment (Figure 2)^[ESMO 2019]
- Early integration of palliative care team for symptom management during treatment both improves quality of life and prolongs survival for patients with advanced NSCLC^[Hau 2017; Temel 2010]

Figure 2. Treatment algorithm for advanced NSCLC (June 2020).^[Osimertinib PI; Erlotinib PI; Afatinib PI; Gefitinib PI; Dacomitinib PI; Alectinib PI; Ceritinib PI; Crizotinib PI; Brigatinib PI; Lorlatinib PI; Entrectinib PI; Dabrafenib PI; Larotrectinib PI; Selpercatinib PI; Capmatinib PI; Nivolumab PI; Pembrolizumab PI; Ipilimumab PI; Atezolizumab PI; Ramucirumab PI; Necitumumab PI; Hanna 2020]



†Also indicated for PD-L1–stained tumor-infiltrating immune cells covering ≥ 10% of tumor area.

‡Single-agent pembrolizumab approved for ≥ 1% PD-L1 but not broadly recommended by experts for < 50% PD-L1 expression.

§Nivolumab + ipilimumab approved for ≥ 1% PD-L1.

For an online Interactive Decision Support Tool for advanced NSCLC showing recommendations from 5 experts for hundreds of patient scenarios, please go to

www.clinicaloptions.com/LungTool

BIOMARKER SUMMARIES

ESTABLISHED BIOMARKERS USED IN STANDARD-OF-CARE NSCLC MANAGEMENT

EGFR Mutations: Aberrant activation of EGFR leads to inhibition of tumor cell apoptosis^[da Cunha Santos 2011]

- ~ 17% incidence in nonsquamous NSCLC^[Tsao 2016]
- Primary testing assays and platforms include:** PCR, NGS^[Lindeman 2018]
 - Testing for mutated EGFR using IHC or *EGFR* alterations using FISH is not recommended^[Lindeman 2018]

Table 2. FDA-Approved Agents for EGFR Mutation-Positive NSCLC^[Afatinib PI; Dacomitinib PI; Erlotinib PI; Gefitinib PI; Osimertinib PI; Sequist 2013; Yang 2015; Wu 2014; Ramalingam 2017; Soria 2018; Maemondo 2010; Mitsudomi 2010; Mok 2018; Wu 2017; Zhou 2011; Zhou 2015; Rosell 2012; Khozin 2014]

Agent	Indication	Dosing	Efficacy
Afatinib	First line+	40 mg PO QD (30 mg if severe renal impairment); ≥ 1 hr before or ≥ 2 hrs after food	ORR: ~ 61% Median PFS: ~ 11 mos Median OS: ~ 26 mos
Dacomitinib	First line+	45 mg PO QD (with or without food)	ORR: 75% Median PFS: 14.7 mos Median OS: 34.1 mos
Erlotinib	First line+	150 mg PO QD; do not take with warfarin due to risk of hemorrhage	ORR: ~ 71% Median PFS: ~ 11.4 mos Median OS: ~ 22.8 mos
Gefitinib	First line+	250 PO QD (with or without food)	ORR: ~ 68% Median PFS: ~ 10.2 mos Median OS: ~ 32.7 mos
Osimertinib	- First line - After EGFR TKI as first-line therapy if positive for <i>EGFR</i> T790M mutation	80 mg PO QD (with or without food)	ORR: 80% (in first line) Median PFS: 18.9 mos Median PFS with CNS mets: 15.2 mos Median OS: not reached

ALK Rearrangements: Fusion of *ALK* and another gene, leading to impaired apoptosis and abnormal cell proliferation^[Fauchinetti 2016]

- ~ 7% incidence in nonsquamous NSCLC^[Tsao 2016]
- Primary testing assays and platforms include:** NGS, FISH, IHC^[Lindeman 2018]
 - FISH is better suited than molecular testing to detect the spectrum of variants of *ALK* rearrangements

Table 3. FDA-Approved Agents for ALK Rearrangement-Positive NSCLC^[Alectinib PI; Brigatinib PI; Ceritinib PI; Crizotinib PI; Lorlatinib PI; Solomon 2014; Solomon 2017; Soria 2017; Nishio 2020; Peters 2017; Camidge 2018a; Camidge 2018b; Camidge 2019a; Camidge 2019b]

Agent	Indication	Dosing	Efficacy
Afatinib	First line+	600 mg BID (with food)	ORR: 83% Median PFS: 34.8 mos Median PFS with CNS mets: 27.7 mos Median OS: not evaluable
Brigatinib	First line+	90 mg QD (7 days), then 180 mg QD as tolerated	ORR: 71% (ICR: 78%) Median PFS: not reached 1-yr PFS: 67% PFS with CNS mets: not reached
Ceritinib	First line+	450 mg QD (with food)	ORR: 68% Median PFS: 16.6 mos Median OS: 51.3 mos
Crizotinib	First line+	250 mg BID	ORR: 74% Median PFS: 10.9 mos Median OS: not reached
Lorlatinib	- After crizotinib and ≥ 1 other ALK inhibitor - After alectinib or ceritinib as first-line therapy	100 mg QD	ORR: 48% (ICR: 60%) Median DoR: 12.5 mos Median intracranial DoR: 19.5 mos

ICR, intracranial response.

ROS1 Rearrangements: Activating *ROS1* gene rearrangements drive transformation and promote proliferation and survival of tumor cells^[Sehgal 2018]

- ~ 2% incidence in nonsquamous NSCLC^[Tsao 2016]
- Primary testing assays and platforms include:** IHC, NGS, targeted high-throughput sequencing gene panels^[Lindeman 2018]
 - Positive ROS1 IHC results should be confirmed by a molecular or cytogenetic method
 - FISH is better suited than molecular testing to detect the spectrum of variants of *ROS1* rearrangements

Table 4. FDA-Approved Agents for *ROS1* Rearrangement-Positive NSCLC^[Crizotinib PI; Entrectinib PI; Shaw 2019; Drilon 2020a]

Agent	Indication	Dosing	Efficacy
Crizotinib	First line+	250 mg BID (200 mg BID for moderate hepatic impairment; 250 mg QD for severe hepatic or renal impairment)	ORR: 72% Median PFS: 19.3 mos Median OS: 51.4 mos
Entrectinib	First line+	600 mg QD	ORR: 77% (ICR: 55%) Median PFS: 19.0 mos Median OS: not estimable

***BRAF* V600E Mutations:** The *BRAF* V600E mutation leads to constitutive activation, increased cell proliferation, and suppression of apoptosis^[Dankner 2018]

- ~ 2% incidence in nonsquamous NSCLC^[Tsao 2016]
- **Primary testing assays and platforms include:** NGS, qualitative detection of single nucleotide variants and deletions in a gene panel including *BRAF* V600E^[Lindeman 2018]

Table 5. FDA-Approved Agents for *BRAF* V600E Mutation-Positive NSCLC^[Dabrafenib PI; Planchard 2016; Planchard 2017]

Agent	Indication	Dosing	Efficacy
Dabrafenib + trametinib	First line+	150 mg BID (1 hr before or 2 hrs after food)	<i>Newly diagnosed metastatic NSCLC</i> ■ ORR: 64% ■ Median PFS: 10.9 mos <i>Previously treated metastatic NSCLC</i> ■ ORR: 63% ■ Median PFS: 9.7 mos

***NTRK* Fusions:** The neurotrophin receptor kinase family consists of 3 TRK proteins that are rarely expressed outside of neuronal tissue; *NTRK* gene fusions lead to constitutive activity as oncogenic drivers across multiple cancers, including NSCLC^[Amatu 2016]

- 0.23% incidence in NSCLC^[Farago 2018]
- **Primary testing assays and platforms include:** IHC, DNA NGS, RNA NGS, FISH, RT-PCR^[Penault-Llorca 2019]
 - Reflexing to NGS vs IHC reasonable for NSCLC due to low prevalence of *NTRK* fusions
 - Diagnostic tests used to identify *NTRK* fusions will also identify many other gene aberrations and potential therapeutic options

Table 6. FDA-Approved Agents for *NTRK* Fusion-Positive NSCLC^[Entrectinib PI; Larotrectinib PI; Farago 2019; Paz-Ares 2019; Drilon 2020b]

Agent	Indication	Dosing	Efficacy
Entrectinib	First line+	<i>Adults:</i> 600 mg QD <i>Children ≥ 12 yrs of age based on BSA</i> ■ BSA > 1.50 m²: 600 mg QD ■ BSA 1.11-1.50 m²: 500 mg QD ■ BSA 0.91-1.10 m²: 400 mg QD	ORR: 70%
Larotrectinib	First line+	<i>Adults with BSA ≥ 1.0 m²:</i> 100 mg BID <i>Children based on BSA:</i> ■ BSA ≥ 1.0 m²: 100 mg BID ■ BSA < 1.0 m²: 100 mg/m² BID	ORR: 75%

BSA, body surface area.

PD-L1: PD-L1 interacts with PD-1 to prevent cytotoxic T-cell responses against tumor cells; PD-L1 expression in tumors suggests the patient may benefit from ICI^[Yu 2016]

- ~ 35% incidence of PD-L1 positivity (PD-L1 ≥ 1%) in nonsquamous NSCLC^[Aggarwal 2016; Pawelczyk 2019]
- PD-L1 positivity can coincide with driver mutation positivity^[Mazières 2019]
 - Patients with PD-L1-positive, *EGFR*-mutated NSCLC should **not** receive ICI due to lack of efficacy and potentially increased risk of toxicity, including fatal pneumonitis, when *EGFR* TKI therapy precedes ICI^[Lisberg 2018; Schoenfeld 2019]
- **Primary testing assays and platforms include:** IHC

Table 7. FDA-Approved Agents for PD-L1-Positive NSCLC^[Atezolizumab PI; Herbst 2019; Pembrolizumab PI; Reck 2016; Reck 2019; Nivolumab PI; Hellmann 2019]

Agent	Indication	Dosing	Efficacy
Atezolizumab	First line for PD-L1 TPS ≥ 50% or PD-L1-positive immune cells covering ≥ 10% of tumor area; no <i>EGFR</i> or <i>ALK</i> genomic aberration	840 mg Q2W, 1200 mg Q3W, or 1680 mg Q4W by IV	ORR: 38% Median PFS: 8.1 mos Median OS: 20.2 mos
Pembrolizumab	First line for PD-L1 TPS ≥ 50%*; no <i>EGFR</i> or <i>ALK</i> genomic aberration	200 mg Q3W or 400 mg Q6W by IV	ORR: 44.8% Median PFS: 10.3 mos Median OS: 30.0 mos
Nivolumab/ipilimumab	First line for PD-L1 TPS ≥ 1%; no <i>EGFR</i> or <i>ALK</i> genomic aberration	Nivolumab: 3 mg/kg Q2W by IV Ipilimumab: 1 mg/kg Q6W by IV	ORR: 36% Median PFS: 5.1 mos Median OS: 17.1 mos

*Approved for PD-L1 ≥ 1% but not broadly recommended by experts for < 50% PD-L1 expression based on clinical data.

- ICIs approved for advanced NSCLC regardless of PD-L1 status include: atezolizumab, nivolumab, nivolumab/ipilimumab, and pembrolizumab^[Atezolizumab PI; Ipilimumab PI; Nivolumab PI; Pembrolizumab PI]
- Indications can be monotherapy or in combination with chemotherapy, and vary across settings (please refer to Table 2)

For an online Interactive Decision Support Tool adapted from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Managing Immune Checkpoint Inhibitor–Related Toxicities, please go to:

www.clinicaloptions.com/immuneAETool

NEW BIOMARKERS IN ADVANCED NSCLC CARE

RET Fusions: Gene rearrangements of *RET* can drive oncogenesis^[Santoro 2013]

- **Primary testing assays and platforms include**^[Lindeman 2018]: DNA NGS, RNA NGS, RT-PCR, expression imbalance
 - Majority of *RET* fusions can be detected by DNA NGS but increased sensitivity with RNA NGS
 - IHC not recommended; FISH recommended only in rare circumstances

Table 8. FDA-Approved Agents for *RET* Fusion–Positive NSCLC^[Selpercatinib PI; Drilon 2019]

Agent	Indication	Dosing	Efficacy	AEs in LIBRETTO-001 Safety Database (N = 531)*
Selpercatinib (LOXO-292)	First line+	Adults and children ≥ 12 yrs of age based on weight: ■ Weight > 50 kg: 120 mg PO BID ■ Weight ≥ 50 kg: 150 mg PO BID ■ Reduce dose in patients with severe hepatic impairment	<i>Treatment naive (n = 34):</i> ■ ORR: 85% ■ Median DoR: not reached ■ Median PFS: not reached <i>Prior platinum doublet chemotherapy (n = 105):</i> ■ ORR: 68% ■ Median DoR: 20.3 mos ■ Median PFS: 18.4 mos CNS ORR (n = 11): 91%	Dry mouth: any, 27% Diarrhea: any, 16%; grade 3/4, 1% Hypertension: any, 18%; grade 3/4, 8% AST ↑: any, 22%; grade 3/4, 5% ALT ↑: any, 21%; grade 3/4, 7% Fatigue: any, 14%; grade 3/4, < 1% Constipation: any, 11%; grade 3/4, < 1% Headache: any, 7%; grade 3/4, < 1% Nausea: any, 8%; grade 3/4, < 1% Peripheral edema: any, 10% Creatinine ↑: any, 10%

*Includes all tumor types (eg, NSCLC, MTC, thyroid, other).

Table 9. Key Ongoing Clinical Trials of Selective *RET* Inhibitors in NSCLC With *RET* Fusions

Agent	Trial*	Phase	Study Population	Preliminary Response Outcomes
Selpercatinib (LOXO-292)	LIBRETTO-001 (NCT03157128)	I/II	<i>RET</i> -altered, advanced solid tumors, including NSCLC	Please refer to Table 8
	LIBRETTO-431 (NCT04194944)	III (vs plt-based CT)	First-line advanced/metastatic <i>RET</i> fusion–positive NSCLC	Results pending
Pralsetinib (BLU-667)	ARROW (NCT03037385)	I/II	<i>RET</i> -altered, advanced solid tumors, including NSCLC	ORR: 60% prior plt (n = 35), 71% treatment naive (n = 7); ICR: 78% (n = 9) ^[Gainer 2019]
	AcceleRET (NCT04222972)	III (vs plt-based CT)	First-line advanced/metastatic <i>RET</i> fusion–positive NSCLC	Results pending

*All recruiting as of June 16, 2020.

MET Exon 14 Skipping Mutations: Splicing mutations lead to exon 14 skipping and loss of ubiquitin-mediated degradation of HGFR, the protein encoded by *MET*; activation of HGFR drives oncogenesis by promoting cell survival and proliferation^[Drilon 2016]

- **Primary testing assays and platforms include:** DNA NGS, RNA NGS, RT-PCR, PCR^[Lindeman 2018]
 - Majority of *MET* exon 14 skipping mutations can be detected with DNA NGS but increased sensitivity with RNA NGS
 - IHC and FISH not recommended

Table 10. FDA-Approved Agents for *MET* Exon 14 Mutation–Positive NSCLC^[Capmatinib PI; Wolf 2019]

Agent	Indication	Dosing	Efficacy	AEs in All Patients With <i>MET</i> -Dysregulated NSCLC* (N = 334)
Capmatinib (INC280)	First line+	400 mg PO BID (with or without food)	<i>Treatment naive (n = 28):</i> ■ ORR: 67.9% ■ Median DoR: 11.1 mos ■ Median PFS: 9.7 mos <i>Prior second/third-line therapy (n = 69):</i> ■ ORR: 40.6% ■ Median DoR: 9.7 mos ■ Median PFS: 5.4 mos CNS ORR (n = 13): 54%	Peripheral edema†: any, 41.6%; grade 3/4, 7.5% Nausea: any, 33.2%; grade 3/4, 1.8% Creatinine ↑: any, 19.5%; grade 3/4, 0 Vomiting: any, 18.9%; grade 3/4, 1.8% Fatigue: any, 13.8%; grade 3/4, 3.0% Appetite ↓: any, 12.6%; grade 3/4, 0.9% Diarrhea: any, 11.4%; grade 3/4, 0.3%

*Including patients with *MET*-mutated or *MET*-amplified NSCLC. †Common class effect. ‡Known to inhibit creatinine transporters.

Table 11. Key Ongoing Clinical Trials of MET Inhibitors in NSCLC With *MET* Exon 14 Skipping Mutations

Agent	Trial	Phase	Study Population	Preliminary Response Outcomes
Highly selective <i>MET</i> inhibitors				
Capmatinib (INC280)	GEOMETRY* (NCT02414139)	II	<i>MET</i> exon 14–altered advanced NSCLC (<i>EGFR</i> WT and <i>ALK</i> negative)	Please refer to Table 9
Tepotinib	VISION* (NCT02864992)	II	Advanced <i>MET</i> -altered NSCLC, including a <i>MET</i> exon 14–altered cohort	ORR [†] : 45.2%/45.5% prior second/third-line tx (n = 31/33); 58.8%/44.4% treatment naive (n = 17/18); intracranial activity observed [‡] [Paik 2019]
Multikinase inhibitors				
Crizotinib*	PROFILE 1001 [§] (NCT00585195)	I	Advanced malignancies, including a <i>MET</i> exon 14–altered NSCLC expansion cohort	ORR: 32% (n = 52) [Drilon 2020a]
	CROME (NCT04084717)	II	<i>ROS1</i> -rearranged, <i>MET</i> exon 14–altered, or <i>MET</i> -amplified advanced NSCLC	Results pending

*Recruiting as of June 16, 2020. [†]First value by liquid biopsy, second value by tissue biopsy. ^{||}Not yet recruiting as of June 16, 2020. [‡]FDA approved indications for *ALK*-positive and *ROS*-positive NSCLC. [§]Active, not recruiting as of June 16, 2020.

OTHER EMERGING BIOMARKERS

- Additional targeted agents are under development for additional driver mutations in advanced NSCLC, all of which are typically reported as part of comprehensive NGS biomarker testing

Table 12. Key Ongoing Trials of Targeted Therapies in NSCLC With Other Emerging Genomic Alterations^[Fakih 2019; Biernacka 2016; Tsao 2016; Baraibar 2020]

Mutation	Incidence	Investigational Agents	Ongoing Trials
<i>KRAS</i>^{G12C*}	13%	■ AMG510 ■ MRTX849	■ NCT03600883, NCT04185883, NCT04303780 ■ NCT03785249, NCT04330664
<i>EGFR/HER2</i> exon 20 insertions	0.3% to 3.7%/ 2% to 4%	■ Pozotinib ■ Mobocertinib (TAK-788) ■ Pyrotinib ■ JNJ-6372	■ NCT03066206, NCT03318939, NCT04044170 ■ NCT04129502 ■ NCT04063462 ■ NCT02609776, NCT04077463
<i>HER2</i> mutations, including exon 20 insertions	2% to 4% [†]	■ Trastuzumab/pertuzumab ■ Trastuzumab deruxtecan	■ NCT03845270 ■ NCT03505710

*Incidence of *KRAS* mutations in NSCLC: 25% to 33%. [†]90% of *HER2* mutations are in exon 20.

References

- Afatinib PI.
- Aggarwal. ESMO 2016. Abstr 1060P.
- Alectinib PI.
- Amatu. ESMO Open. 2016;1:e000023.
- Atezolizumab PI.
- Baraibar. Crit Rev Oncol Hematol. 2020;148:102906.
- Bernabé. Eur J Cancer. 2017;81:66.
- Bernicker. J Oncol Pract. 2017;13:221.
- Biernacka. Cancer Genet. 2016;209:195.
- Brigatinib PI.
- Camidge. ASCO 2018a. Abstr 9043.
- Camidge. NEJM. 2018b;379:2027.
- Camidge. JTO. 2019a;14:1233.
- Camidge. ESMO Asia Congress 2019b.
- Capmatinib PI.
- Ceritinib PI.
- Crizotinib PI.
- da Cunha Santos. Annu Rev Pathol. 2011;6:49.
- Dabrafenib PI.
- Dacomitinib PI.
- Dankner. Oncogene. 2018;37:31183.
- Doxtader. Arch Pathol Lab Med. 2019;143:670.
- Drilon. Clin Cancer Res. 2016;22:2832.
- Drilon. WCLC 2019. Abstr PL02.08.
- Drilon. Nat Med. 2020a;26:47.
- Drilon. Lancet Oncol. 2020b;21:261.
- Entrectinib PI.
- Erlotinib PI.
- ESMO. Available at: <https://www.esmo.org/guidelines/lung-and-chest-tumours/metastatic-non-small-cell-lung-cancer>.
- Facchinetti. Transl Lung Cancer Res. 2016;5:301.
- Fakih. ASCO 2019. Abstr 3003.
- Farago. JPO Precis Oncol. 2018;2018:10.1200/PO.18.00037.
- Farago. WCLC 2019. Abstr MA09.07.
- Gainor. ASCO 2019. Abstr 9008.
- Gandara. ASTRO/ASCO/IASLC Symposium on Molecular Testing. 2012.
- Gefitinib PI.
- Ipilimumab PI.
- Hanna. J Clin Oncol. 2020;[Epub].
- Haun. Cochrane Database Syst Rev. 2017;6:CD011129.
- Hellmann. NEJM. 2019;381:2020.
- Herbst. SITC 2019. Abstr O81.
- Hirsch. Clin Lung Cancer. 2018;19:331.
- Kalemkerian. JCO. 2018;36:911.
- Khozin. Oncologist. 2014;19:774.
- Larotrectinib PI.
- Lindeman. Arch Pathol Lab Med. 2018;142:321.
- Lisberg. J Thorac Oncol. 2018;13:1138.
- Lorlatinib PI.
- Maemondo. NEJM. 2010;362:2380.
- Masters. JCO. 2015;33:3488.
- Mazières. Ann Oncol. 2019;30:1321.
- Mitsudomi. Lancet Oncol. 2010;11:121.
- Mok. JCO. 2018;36:2244.
- Necitumumab PI.
- Nishio. JTO. 2020;15:609.
- Nivolumab PI.
- Noll. Cancer Cytopathol. 2018;126:342.
- Osimertinib PI.
- Paik. ASCO 2019. Abstr 9005.
- Pawelczyk. Int J Mol Sci. 2019; 20:824.
- Paz-Ares. ELCC 2019. Abstr 113O.
- Pembrolizumab PI.
- Penault-Llorca. J Clin Path. 2019;72:460.
- Pennell. Am Soc Clin Oncol Educ Book. 2019;39:531.
- Peters. NEJM. 2017;377:829.
- Planchard. Lancet Oncol. 2016;17:642.
- Planchard. Lancet Oncol. 2017;18:1307.
- Ramalingam. ESMO 2017. Abstr LBA2_PR.
- Ramucirumab PI.
- Reck. NEJM. 2016;375:1823.
- Reck. JCO. 2019;37:537.
- Rosell. Lancet Oncol. 2012;13:239.
- Santoro. Cold Spring Harb Perspect Biol. 2013;5:a009233.
- Schoenfeld. Ann Oncol. 2019;30:839.
- Sehgal. Transl Cancer Res. 2018;7(suppl 7):S779.
- Selpercatinib PI.
- Sequist. J Clin Oncol. 2013;31:3327.
- Shaw. Ann Oncol. 2019;30:1121.
- Solomon. NEJM. 2014;371:2167.
- Solomon. JCO. 2018;36:2251.
- Soria. NEJM. 2018;378:113.
- Temel. NEJM. 2010;363:733.
- Tsao. J Thorac Oncol. 2016;11:613.
- Wolf. ASCO 2019. Abstr 9004.
- Wu. Lancet Oncol. 2014;15:213.
- Wu. Lancet Oncol. 2017;18:1454.
- Yang. Lancet Oncol. 2015;16:141.
- Yu. J Thorac Oncol. 2016;11:964.
- Zhou. Lancet Oncol. 2011;12:735.
- Zhou. Ann Oncol. 2015;26:1877.