

In metastatic EGFRm non-small cell lung cancer (NSCLC)

# Treat the driver of disease

Optimal treatment starts with a complete molecular profile

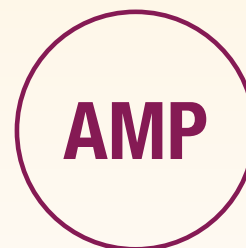
Guidelines recommend treatment plans based on the identification of targetable mutations and demonstrated efficacy and safety<sup>1-3</sup>:



National Comprehensive  
Cancer Network® (NCCN®)



American Society of Clinical  
Oncology® (ASCO®)



Association for Molecular  
Pathology (AMP)



College of American  
Pathologists (CAP)



Society for  
Immunotherapy of  
Cancer (SITC)



International Association  
for the Study of Lung  
Cancer (IASLC)

## In metastatic EGFRm NSCLC

There is no evidence to support treatment with IO as first line in EGFRm patients

### First-line IO trials have excluded treatment-naïve EGFRm patients<sup>4-12</sup>

- Eight out of 9 of the most recognized IO trials **DID NOT** allow treatment-naïve EGFRm patients

Therapy	Trial	Allowed treatment-naïve EGFRm patients
Pembrolizumab monotherapy	KEYNOTE-024	<b>NO</b>
	KEYNOTE-042	<b>NO</b>
	Phase II Study in Advanced NSCLC (NCT02879994)	<b>YES*</b>
Pembrolizumab + doublet chemotherapy	KEYNOTE-021 Cohort G	<b>NO</b>
	KEYNOTE-189	<b>NO</b>
Nivolumab monotherapy	CHECKMATE 026	<b>NO</b>
Nivolumab monotherapy ± ipilimumab or platinum doublet chemotherapy	CHECKMATE 227	<b>NO</b>
Atezolizumab + doublet chemotherapy	IMpower130 <sup>†</sup>	<b>NO</b>
Atezolizumab + bevacizumab + doublet chemotherapy	IMpower150 <sup>†</sup>	<b>NO</b>

### IO or IO and chemo combinations are not being studied in treatment-naïve EGFRm patient populations<sup>4-11</sup>

- There are no head-to-head trials comparing IO and EGFR TKIs in patients with EGFRm NSCLC

### No IO therapies, either as a single agent or in combination, are FDA approved for treatment-naïve EGFRm patients<sup>13-15</sup>

- Pembrolizumab, nivolumab, and atezolizumab are not approved for EGFRm patients

IO, immunotherapy.

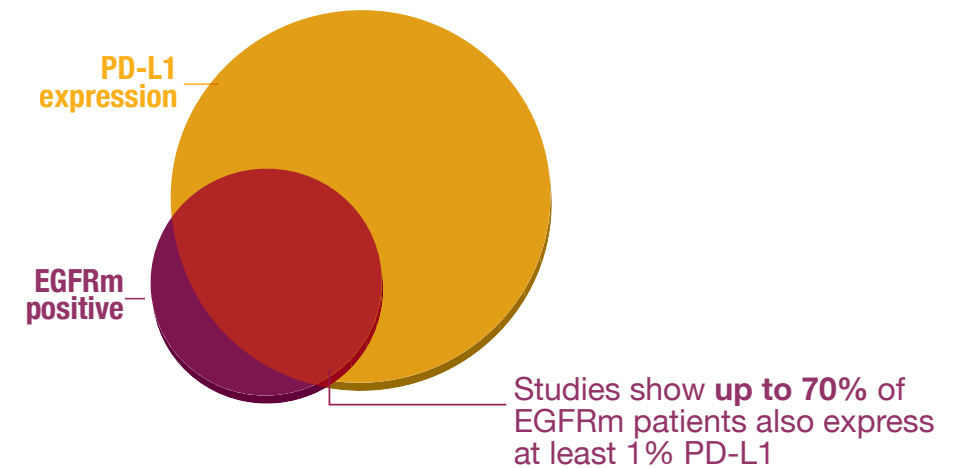
\*First-line pembrolizumab treatment showed no benefit in the 11 patients with EGFR mutation-positive NSCLC, even in patients with PD-L1 expression  $\geq 50\%$ .<sup>6</sup>

<sup>†</sup>EGFRm positive patients were allowed only after progression on EGFR-TKI therapy.<sup>12</sup>

## In metastatic EGFRm NSCLC

EGFR TKIs are the first-line recommended option, independent of PD-L1 expression<sup>1</sup>

EGFR mutation status and PD-L1 expression are not mutually exclusive<sup>16-19</sup>



### Prospective IO monotherapy study in EGFRm TKI-naïve NSCLC; enrollment ceased due to lack of efficacy<sup>6</sup>

- In a Phase II study (NCT02879994) enrollment was ceased due to lack of efficacy after 11 of 25 planned patients were treated. No responses were observed in the 10 patients with EGFRm NSCLC even though most patients were PD-L1 high (TPS  $\geq 50\%$ )<sup>6</sup>
  - One patient with EGFR WT NSCLC had a response

### AFTER treatment with an EGFR TKI, IO is an option in EGFRm patients (IO/chemo combo, or IO after a subsequent chemo combo)<sup>1,3</sup>

- Treatment guidelines recommend the use of IO in EGFRm patients only after EGFR TKI therapies have been exhausted<sup>3</sup>
  - SITC Guidelines recommend IO only after targeted therapy and chemotherapy<sup>3</sup>

## In metastatic EGFRm non-small cell lung cancer (NSCLC)

# EGFR TKIs are the first-line recommended option, independent of PD-L1 expression<sup>1</sup>

## Without a full molecular profile, patients may not receive optimal treatment

- Several guidelines recommend testing for appropriate genetic targets and treating with targeted therapy based on test results<sup>1-3</sup>
- Patients may have both an EGFR mutation and PD-L1 expression<sup>18</sup>
- First-line IO trials have excluded treatment-naïve EGFRm patients<sup>6</sup>
- IO is not approved or indicated in the first-line EGFRm NSCLC setting<sup>4-12</sup>
- Data in a few patients suggest that pembrolizumab monotherapy is not effective as first-line therapy in patients with metastatic NSCLC and EGFR mutations, even those with PD-L1  $\geq 50\%$ <sup>1</sup>

**References:** 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for NSCLC V.3.2019. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed January 22, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 2. Kalemkerian GP, Narula N, Kennedy EB, et al. Molecular testing guideline for the selection of patients with lung cancer for treatment with targeted tyrosine kinase inhibitors: American Society of Clinical Oncology endorsement of the College of American Pathologists/International Association for the Study of Lung Cancer/Association for Molecular Pathology Clinical Practice Guideline update. *J Clin Oncol*. 2018;36(9):911-919. 3. Brahmer JR, Govindan R, Anders RA, et al. The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of non-small cell lung cancer (NSCLC). *J Immunother Cancer*. 2018;6(1):75. 4. Reck M, Rodríguez-Abreu D, Robinson AG, et al; KEYNOTE-024 Investigators. Pembrolizumab versus chemotherapy for PD-L1–positive non–small-cell lung cancer. *N Engl J Med*. 2016;375(19):1823-1833. 5. Clinicaltrials.gov. Study of MK-3475 (pembrolizumab) versus platinum-based chemotherapy for participants with PD-L1-positive advanced or metastatic non-small cell lung cancer (MK-3475-042/KEYNOTE-042). <https://clinicaltrials.gov/ct2/show/NCT02220894>. Accessed January 9, 2019. 6. Lisberg A, Cummings A, Goldman JW, et al. A phase II study of pembrolizumab in EGFR-mutant, PD-L1–positive, tyrosine kinase inhibitor naïve patients with advanced NSCLC. *J Thorac Oncol*. 2018;13(8):1138-1145. 7. Langer CJ, Gadgeel SM, Borghaei H, et al; KEYNOTE-021 Investigators. Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study. *Lancet Oncol*. 2016;17(11):1497-1508. 8. Broderick JM. Frontline pembrolizumab combo improves survival in phase III NSCLC trial. <https://www.onclive.com/web-exclusives/frontline-pembrolizumab-combo-improves-survival-in-phase-iii-nsclc-trial>. Published January 16, 2018. Updated April 16, 2018. Accessed January 9, 2019. 9. Carbone DP, Reck M, Paz-Ares L, et al; CheckMate 026 Investigators. First-line nivolumab in stage IV or recurrent non–small-cell lung cancer. *N Engl J Med*. 2017;376(25):2415-2426. 10. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. *N Engl J Med*. 2018;378(22):2093-2104. 11. EU Clinical Trials Register. A phase III clinical study to evaluate the efficacy and safety of atezolizumab in combination with carboplatin + nab-paclitaxel compared with carboplatin + nab-paclitaxel in patients with stage IV non-squamous non-small cell lung cancer. EudraCT number 2014-003206-32. <https://www.clinicaltrialsregister.eu/>. Accessed January 28, 2019. 12. Kowanetz M, Socinski MA, Zou W, et al. IMpower150: efficacy of atezolizumab plus bevacizumab and chemotherapy in 1L metastatic nonsquamous NSCLC across key subgroups. Presented at: AACR; April 14-18, 2018; Chicago, IL. 13. Keytruda [package insert]. Whitehouse Station, NJ: Merck & Co., Inc; 2018. 14. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc; 2018. 15. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2018. 16. Akamine T, Takada K, Toyokawa G, et al. Association of preoperative serum CRP with PD-L1 expression in 508 patients with non-small cell lung cancer: a comprehensive analysis of systemic inflammatory markers. *Surg Oncol*. 2018;27(1):88-94. 17. Liu SY, Dong ZY, Wu SP, et al. Clinical relevance of PD-L1 expression and CD8+ T cells infiltration in patients with EGFR-mutated and ALK-rearranged lung cancer. *Lung Cancer*. 2018;125:86-92. 18. Yoneshima Y, Ijichi K, Anai S, et al. PD-L1 expression in lung adenocarcinoma harboring EGFR mutations or ALK rearrangements. *Lung Cancer*. 2018;118:36-40. 19. D'Incecco A, Andreozzi M, Ludovini V, et al. PD-1 and PD-L1 expression in molecularly selected non-small-cell lung cancer patients. *Br J Cancer*. 2015;112(1):95-102.