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\(^1-3\):

- **NCCN**
  - National Comprehensive Cancer Network\(^{\text{®}}\) (NCCN\(^{\text{®}}\))

- **ASCO**
  - American Society of Clinical Oncology\(^{\text{®}}\) (ASCO\(^{\text{®}}\))

- **AMP**
  - Association for Molecular Pathology (AMP)

- **CAP**
  - College of American Pathologists (CAP)

- **SITC**
  - Society for Immunotherapy of Cancer (SITC)

- **IASLC**
  - 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\(^4\)\(^-\)\(^12\)

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Trial</th>
<th>Allowed treatment-naïve EGFRm patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab monotherapy</td>
<td>KEYNOTE-024</td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td>KEYNOTE-042</td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td>Phase II Study in Advanced NSCLC</td>
<td>YES*</td>
</tr>
<tr>
<td>Pembrolizumab + doublet chemotherapy</td>
<td>KEYNOTE-021 Cohort G</td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td>KEYNOTE-189</td>
<td>NO</td>
</tr>
<tr>
<td>Nivolumab monotherapy</td>
<td>CHECKMATE 026</td>
<td>NO</td>
</tr>
<tr>
<td>Nivolumab monotherapy + ipilimumab or platinum doublet chemotherapy</td>
<td>CHECKMATE 227</td>
<td>NO</td>
</tr>
<tr>
<td>Atezolizumab + doublet chemotherapy</td>
<td>IMpower130(^2)</td>
<td>NO</td>
</tr>
<tr>
<td>Atezolizumab + bevacizumab + doublet chemotherapy</td>
<td>IMpower150(^2)</td>
<td>NO</td>
</tr>
</tbody>
</table>

IO or IO and chemo combinations are not being studied in treatment-naïve EGFRm patient populations\(^4\)\(^-\)\(^11\)

- 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\(^13\)\(^-\)\(^15\)

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

EGFR TKIs are the first-line recommended option, independent of PD-L1 expression\(^1\)

EGFR mutation status and PD-L1 expression are not mutually exclusive\(^16\)\(^-\)\(^19\)

Studies show up to 70% of EGFRm patients also express at least 1% PD-L1

Prospective IO monotherapy study in EGFRm TKI-naïve NSCLC; enrollment ceased due to lack of efficacy\(^6\)

- 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 ≥50%)\(^6\)
  - 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)\(^1\)\(^3\)

- Treatment guidelines recommend the use of IO in EGFRm patients only after EGFR TKI therapies have been exhausted\(^2\)
  - SITC Guidelines recommend IO only after targeted therapy and chemotherapy\(^3\)

\(^{*}\)First-line pembrolizumab treatment showed no benefit in the 11 patients with EGFR mutation-positive NSCLC, even in patients with PD-L1 expression ≥50%\(^6\)

\(^{†}\)EGFRm positive patients were allowed only after progression on EGFR-TKI therapy.\(^1\)
In metastatic EGFRm non-small cell lung cancer (NSCLC)

EGFR TKIs are the first-line recommended option, independent of PD-L1 expression

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
- Patients may have both an EGFR mutation and PD-L1 expression
- First-line IO trials have excluded treatment-naive EGFRm patients
- IO is not approved or indicated in the first-line EGFRm NSCLC setting
- 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 ≥50%