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NCCN Guidelines Panel: Non-Small Cell Lung Cancer

Dear NCCN Guidelines Panel for Non-Small Cell Lung Cancer,

Request:¹⁻²

Please consider the following Food and Drug Administration (FDA) approval for Tecentriq® (atezolizumab) for inclusion into the guideline.

Based on the IMpower110 trial, Tecentriq received FDA approval on May 18, 2020 for first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (PD-L1 stained $\geq 50\%$ of tumor cells [TC $\geq 50\%$] or PD-L1 stained tumor-infiltrating immune cells [IC] covering $\geq 10\%$ of the tumor area [IC $\geq 10\%$]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

The IMpower110 interim analysis presented at the 2019 European Society for Medical Oncology (ESMO) Congress was previously submitted to NCCN in September 2019. Outcomes in patients with high PD-L1 expression (TC $\geq 50\%$ or IC $\geq 10\%$) were considered final at the time of interim analysis.

Rationale:²⁻⁴

IMpower110 was a Phase 3 trial conducted to evaluate the efficacy and safety of Tecentriq monotherapy compared with platinum-based chemotherapy as first-line treatment for patients with chemotherapy-naïve, PD-L1-selected, metastatic NSCLC, independent of tumor histology. The primary endpoint was overall survival (OS), sequentially tested in the following subgroups of patients, excluding those with EGFR or ALK genomic tumor aberrations: TC $\geq 50\%$ or IC $\geq 10\%$; TC $\geq 5\%$ or IC $\geq 5\%$; and TC $\geq 1\%$ or IC $\geq 1\%$.

- At the time of interim analysis, median survival follow-up time was 15.7 months. Tecentriq monotherapy (n=107) demonstrated a statistically significant improvement in OS for patients with high PD-L1 expression (TC $\geq 50\%$ or IC $\geq 10\%$), showing prolonged median OS compared to chemotherapy (n=98; 20.2 vs. 13.1 months, respectively; HR=0.59 [95% CI, 0.40-0.89], p=0.0106).
- There was no statistically significant difference in OS for the TC $\geq 5\%$ or IC $\geq 5\%$ and TC $\geq 1\%$ or IC $\geq 1\%$ subgroups at the interim or final analyses.

In a pre-specified, exploratory analysis, consistency in efficacy outcomes were observed across high PD-L1 expression subgroups regardless of assay used (VENTANA PD-L1 (SP142) and (SP263) Assays, and the Dako PD-L1 22C3 pharmDx). Median OS in the high PD-L1 expression subgroups favored treatment with Tecentriq regardless of assay used. Please refer to the enclosed presentation from the 2019 ESMO Immuno-Oncology Congress for additional details.

Overall, the safety profile for Tecentriq was consistent with prior observations, with no new safety signals identified. Fatal adverse reactions occurred in 3.8% of patients receiving Tecentriq; these included death (reported as unexplained death and death of unknown cause), aspiration, chronic obstructive pulmonary disease, pulmonary embolism, acute myocardial infarction, cardiac arrest, mechanical ileus, sepsis, cerebral infarction, and device occlusion (1 patient each). Serious adverse reactions occurred in 28% of patients receiving Tecentriq, with the most frequent serious adverse reactions ($>2\%$) being pneumonia (2.8%), chronic obstructive pulmonary disease (2.1%) and pneumonitis (2.1%). Tecentriq was

discontinued due to adverse reactions in 6% of patients, of which the most common (≥ 2 patients) leading to Tecentriq discontinuation were peripheral neuropathy and pneumonitis.

FDA Clearance:²

- The aforementioned data reflect an FDA-approved use for Tecentriq. Please refer to the product prescribing information for the full FDA-approved indications and safety information, available at: https://www.gene.com/download/pdf/tecentriq_prescribing.pdf

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Thank you for your consideration and I hope this information is helpful to you. If you have any questions, please contact us at the phone number and email provided above.

Respectfully submitted,
Neda Nguyen, PharmD

References:

1. FDA Approves Genentech's Tecentriq as First-Line Monotherapy for Certain People With Metastatic Non-Small Cell Lung Cancer [Press Release]. South San Francisco, CA; Genentech, Inc. May 18, 2020. Accessed from: <https://www.gene.com/media/press-releases/14850/2020-05-18/fda-approves-genentechs-tecentriq-as-a-f>
2. Tecentriq® [package insert]. South San Francisco, CA: Genentech, Inc.; 2020.
3. Spigel DR, De Marinis F, Giaccone G et al. IMpower110: Interim OS Analysis of a Phase III Study of Atezolizumab (atezo) vs Platinum-Based Chemotherapy (chemo) as 1L Treatment (tx) in PD-L1–selected NSCLC. Presented at the European Society for Medical Oncology (ESMO) 2019. Congress in Barcelona, Spain; Sept 27-Oct 1, 2019. ESMO Abstract #LBA78. Abstract available at: <https://oncologypro.esmo.org/meeting-resources/esmo-2019-congress/IMpower110-Interim-overall-survival-OS-analysis-of-a-phase-III-study-of-atezolizumab-atezo-vs-platinum-based-chemotherapy-chemo-as-first-line-1L-treatment-tx-in-PD-L1-selected-NSCLC>.
4. Herbst R, De Marinis F, Giaccone G, et al. Clinical Efficacy of Atezolizumab in Biomarker Subgroups by SP142, SP263 and 22C3 PD-L1 Immunohistochemistry Assays and by Blood Tumour Mutational Burden: Results From the IMpower110 Study. Presented at the 2019 European Society For Medical Oncology (ESMO) Immuno-Oncology Congress in Geneva, Switzerland; Dec 11-14, 2019. ESMO IO Oral Presentation. Abstract available at: <https://oncologypro.esmo.org/meeting-resources/esmo-immuno-oncology-congress-2019/clinical-efficacy-of-atezolizumab-atezo-in-biomarker-subgroups-by-sp142-sp263-and-22c3-pd-l1-immunohistochemistry-ihc-assays-and-by-blood-tumour-mutational-burden-btmb-results-from-the-impower110-study>.