Genentech
A Member of the Roche Group

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NCCN Non-Small Cell Lung Cancer

Dear NCCN Guidelines Panel,

On behalf of Genentech, Inc., the FDA approval and previously presented data from the Phase III IMpower110 study evaluating Tecentriq® (atezolizumab) monotherapy for the first-line treatment of programmed death ligand-1 (PD-L1)-selected non-small cell lung cancer (NSCLC) was previously submitted to NCCN in June 2020.[1-3] As follow-up, IMpower110 trial results are now published in the New England Journal of Medicine, and are enclosed for your review and updating needs.[1]

Request:

Please consider upgrading Tecentriq monotherapy to a Category 1, Preferred option for first-line therapy in patients with PD-L1 expression positive (≥ 50%) advanced or metastatic NSCLC (NSCL-30, NSCL-I 1 of 2, relevant discussion sections [MS-60-61], and references).

Rationale:

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.[1] Data from the Phase III IMpower 110 study have previously been presented.[2,3]

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 ≥ 50% or IC ≥ 10%; TC ≥ 5% or IC ≥ 5%; and TC ≥ 1% or IC ≥ 1%.[1]

Efficacy:[1]

- A total of 572 patients were randomized to receive either Tecentriq monotherapy or platinum-based chemotherapy. The population with EGFR and ALK wild-type tumors comprised 554 patients (277 patients in each group).
- Overall, in the population with EGFR and ALK wild-type tumors, 107 patients (38.6%) in the Tecentriq monotherapy group and 98 (35.4%) in the chemotherapy group had high expression of PD-L1.
- 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 ≥ 50% or IC ≥ 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=0.01).
- There was no statistically significant difference in OS for the TC ≥ 5% or IC ≥ 5% and TC ≥ 1% or IC ≥ 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 (Fig 2A-C).

Safety:[1]

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 in the Tecentriq arm and 4.2% of patients in the chemotherapy arm. Grade 3 or 4 adverse events were reported in 30.1% of patients receiving Tecentriq and 52.5% of patients receiving chemotherapy. The most common Grade 3 or 4 adverse events occurring in >2% of patients in the Tecentriq arm included hyponatremia (2.1%), hyperkalemia (2.1%), and pneumonia (2.4%). Grade 3 or 4 immune-mediated adverse events, regardless of whether they required treatment with systemic glucocorticoids, endocrine therapy, or other immunosuppressants, occurred in 6.6% of patients receiving Tecentriq. Please refer to Tables 2, S7, and S9 for the full list of adverse events.

FDA Clearance:[4]

- 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

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,
Aileen Le, Pharm.D, BCPS

References

1. Herbst RS, Giaccone G, de Marinis F, et al. Atezolizumab for First-LineTreatment of PD-L1-Selected Patients with NSCLC. N Engl J Med2020;383:1328-1339. https://www.ncbi.nlm.nih.gov/pubmed/32997907

2. 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.

3. 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

4. Tecentriq® [package insert]. South San Francisco, CA: Genentech, Inc.; 2020.