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A Member of the Roche Group

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NCCN Guidelines Panel: Non-Small Cell Lung Cancer (NSCLC)

Dear NCCN Guidelines Panel for NSCLC:

On behalf of Genentech, Inc. enclosed are interim analysis results from the Phase III IMpower010 study evaluating the efficacy and safety of adjuvant Tecentriq® (atezolizumab) vs best supportive care (BSC) after adjuvant chemotherapy in patients with completely resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC), recently presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting.[1]

Requests:

1. Please consider the enclosed data on the use of atezolizumab as adjuvant treatment following resection and platinum-based chemotherapy for patients with NSCLC, for inclusion into the NCCN NSCLC Guidelines pages:
    - **NSCL-4, NSCL-6, NSCL-7: Adjuvant Treatment**, and
    - **NSCL-E: Systemic Therapy Regimens for Neoadjuvant and Adjuvant Therapy**
2. Please include determination of tumor PD-L1 status as a footnote for treatment with atezolizumab, for Stage II to IIIA, operable NSCLC on NCCN NSCLC Guidelines pages:
    - **NSCL-3, NSCL-4, NSCL-6, NSCL-7**: **Clinical Assessment workup and Adjuvant Treatment**

Rationale:

While adjuvant treatment options with platinum-based chemotherapy for patients with resectable early-stage NSCLC (eNSCLC) show a 4-5% overall survival (OS) improvement at 5 years vs observation, approximately half of all patients with early lung cancer still experience a recurrence following surgery.[1-7] There remains a tremendous unmet need for improved adjuvant treatment in NSCLC patients.[1]

IMpower010, a phase III, global, multi-center, open-label, randomized study in previously untreated patients with resectable NSCLC, is the first phase III study to show that a cancer immunotherapy improves disease-free survival (DFS) in this patient population.[1] Key eligibility criteria include patients with ECOG PS 0-1, tumor tissue for PD-L1 analysis, histologically or cytologically confirmed, Stage IB (tumors ≥4 cm) to IIIA NSCLC per AJCC 7th edition.

The primary endpoint is investigator-assessed DFS in 3 primary analysis populations:[1,8]

- The PD-L1 ≥ 1% subpopulation within the Stage II-IIIA population,
- All randomized patients with Stage II-IIIA NSCLC, and
- The intent-to-treat (ITT) population

Key secondary endpoints include Overall Survival (OS) in the ITT population, DFS in the PD-L1 TC ≥50%, Stage II-IIIA population, and 3-year and 5-year DFS.

Efficacy[1]

At the time of this pre-specified interim analysis, the study met its primary endpoint in two of three primary analysis populations, providing evidence of clinical efficacy for adjuvant atezolizumab following adjuvant standard of care chemotherapy in resected eNSCLC. Efficacy outcomes after a median follow-up of ~32 months (range, 0-58.8) are presented in the table below. At this interim analysis, atezolizumab showed a statistically significant DFS benefit in the PD-L1 TC ≥1% Stage II-IIIA (stratified HR=0.66; 95% CI, 0.5-0.88) and all-randomized Stage II-IIIA (HR=0.79; 95% CI, 0.64-0.96) populations. The DFS testing boundary was not crossed in the ITT population (Stage IB-IIIA).

Summary of Primary Efficacy Outcomes in the IMpower010 Study*						
Endpoint	PD-L1 TC ≥1%† Stage II-IIIA		All-Randomized Stage II-IIIA		ITT Stage IB-IIIA	
	Atezolizumab (n=248)	BSC (n=228)	Atezolizumab (n=442)	BSC (n=440)	Atezolizumab (n=507)	BSC (n=498)
Disease-free survival						
Median, mo (95% CI)	NE (36.1-NE)	35.3 (29-NE)	42.3 (36-NE)	35.3 (30.4-46.4)	NE (36.1-NE)	37.2 (31.6-NE)
HR‡ (95% CI)	0.66 (0.5-0.88)		0.79 (0.64-0.96)		0.81 (0.67-0.99)	
p-value§	0.004‖		0.02‖		0.04¶	

Notes: * Data cutoff: January 21, 2021. † Per SP263 assay. ‡ Stratified hazard ratio. § Stratified log-rank. ‖ The statistical significance boundary for DFS was crossed. ¶ The statistical significance boundary for DFS was not crossed.
Abbreviations: BSC=best supportive care; CI=confidence interval; HR=hazard ratio; ITT=intent-to-treat; NE=not evaluable; OS=overall survival; TC=tumor cell.

OS data were immature at this pre-planned DFS interim analysis. While OS in the ITT population was not formally tested at this time, a trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥ 1% Stage II-IIIA population (stratified HR 0.77; 95% CI 0.51, 1.17). IMpower010 will continue for DFS and OS analyses in the ITT population.

Safety[1]

The safety profile of atezolizumab was consistent with prior experience of atezolizumab monotherapy across multiple indications and other lines of therapy. No new or unexpected safety signals were identified.

Treatment-related adverse events of any grade were reported in 67.7% of patients treated with atezolizumab, as shown in the table below. Treatment-related Grade 5 adverse events were reported in 4 (0.8%) patients treated with atezolizumab and included interstitial lung disease, multiple organ dysfunction syndrome, myocarditis, and acute myeloid leukemia. Please refer to the enclosed presentation for further detail.[1]

Safety Summary in the IMpower010 Study*†		
Event Category, %	Atezolizumab (n=495)	BSC (n=495)
Any cause adverse event	92.7	70.7
Treatment-related	67.7	-
Grade 3-4 adverse event	21.8	11.5
Treatment-related	10.7	-
Serious adverse event	17.6	8.5
Treatment-related	7.5	-
Grade 5 adverse event	1.6‡	0.6§
Treatment-related	0.8	-
Adverse event leading to dose interruption of atezolizumab	28.7	-
Adverse event leading to atezolizumab discontinuation	18.2	-
Immune-mediated adverse events	51.7	9.5
Grade 3-4 immune-mediated adverse events	7.9	0.6
Immune-mediated adverse event requiring systemic corticosteroid use	12.1	0.8

Notes: * Data cutoff: January 21, 2021. † Data are from safety population (all randomized patients who received ≥1 atezolizumab dose or for BSC, had ≥1 post-baseline assessment). ‡ Interstitial lung disease (treatment-related); pneumothorax; multiple organ dysfunction syndrome (treatment-related); cerebrovascular accident; arrhythmia; myocarditis (treatment-related); acute myeloid leukemia (treatment-related); acute cardiac failure. § Pneumonia; pulmonary embolism; cardiac tamponade and septic shock in the same patient.

FDA Clearance:

- Tecentriq® (atezolizumab) is not FDA-approved for use as adjuvant therapy in previously untreated patients with resectable NSCLC, and is under investigation in this setting.
- Please refer to the product prescribing information for the full FDA-approved indications and safety information, available at: http://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,
Neda Nguyen, PharmD

References

1. Wakelee HA, Altorki N, Zhou C, et al. IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC). Presented at the American Society of Clinical Oncology Annual Meeting (Virtual); June 4–8, 2021. ASCO Oral Presentation.
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3. Genentech, Inc. (2021, May 19*). Pivotal Phase III Data at ASCO Show Genentech's Tecentriq Helps Certain People With Early Lung Cancer Live Significantly Longer Without Their Disease Returning.* [Press release]. Retrieved from https://www.gene.com/media/press-releases/14910/2021-05-19/pivotal-phase-iii-data-at-asco-show-gene
4. Pignon J-P, et al. J Clin Oncol 2008;26:3552-9
5. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. V8.2020
6. Postmus PE, et al. Ann Oncol 2017;28(suppl 4):iv1-21.
7. Vansteenkiste J, et al. Ann Oncol 2019;30(8):1244-53;
8. Hoffman-La Roche. Study to Assess Safety and Efficacy of Atezolizumab (MPDL3280A) Compared to Best Supportive Care Following Chemotherapy in Patients With Lung Cancer [IMpower010]. 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT02486718. Accessed on May 10, 2021.