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

On behalf of Genentech, Inc., I respectfully request the NCCN NSCLC Guideline Panel to review the enclosed data for:

- Tecentriq™ (Atezolizumab): NSCLC

Fehrenbacher L, Spira A, Ballinger M, et al. Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, Phase 2 randomised controlled trial. *Lancet* 2016;387:1837-46.

Smith D, Vansteenkiste J, Fehrenbacher L, et al. Updated survival and biomarker analyses of a randomized Phase II study of atezolizumab vs docetaxel in previously treated NSCLC (POPLAR). Presented at the American Society of Clinical Oncology 2016 Annual Meeting in Chicago, IL; 2016 Jun 3-7. ASCO Poster 351.

**Specific Changes:**

Consider the available data on the use of Tecentriq in NSCLC for your updating purposes.

**FDA Clearance:**

Tecentriq is not FDA-approved for use in patients with NSCLC.

Tecentriq is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

- Have disease progression during or following platinum-containing chemotherapy
- Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Please refer to the Tecentriq prescribing information for the full FDA-approved indications and safety information.

- Full Tecentriq™ prescribing information available at:  
[http://www.gene.com/download/pdf/tecentriq\\_prescribing.pdf](http://www.gene.com/download/pdf/tecentriq_prescribing.pdf)

**Rationale:**

POPLAR is an open-label, Phase II, randomized study conducted to evaluate the efficacy and safety of Tecentriq compared with docetaxel in 287 patients with locally advanced or metastatic NSCLC who had progressed on platinum-containing chemotherapy. The primary endpoint was overall survival (OS) in the intent-to-treat (ITT) (unselected) population and programmed death-ligand 1 (PD-L1) subgroups. Progression-free survival (PFS), overall response rate (ORR), duration of response (DOR), and safety were secondary endpoints.

**Efficacy**

- At the primary analysis (minimum 13 month follow-up), Tecentriq significantly improved OS in the ITT population. OS was 12.6 months (95% CI 9.7-16.4) for Tecentriq compared with 9.7 months

for docetaxel (95% CI 8.6-12.0) [Hazard ratio (HR) 0.73, 95% CI 0.53-0.99; p=0.04]. Although median OS did not change in an updated analysis (minimum 20 months follow-up), the OS HR in the ITT population improved [HR: 0.69; 95% CI 0.52-0.92; p=0.011].

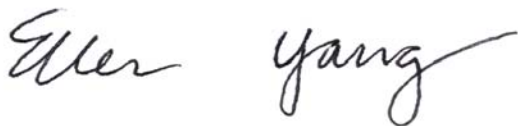
- Improvement in OS HR was observed across all PD-L1 subgroups for Tecentriq compared with docetaxel at the updated analysis. Of note, OS improvement favored Tecentriq in the TC0 (tumor cells) or IC0 (tumor-infiltrating immune cells) subgroup over docetaxel (HR: 0.88; 95% CI 0.55-1.42; p=0.60).
- In the ITT updated analysis, PFS in the Tecentriq-treated arm was 2.7 months (95% CI 2.0-4.1) compared with 3.4 months (95% CI 2.8-4.1) in the docetaxel-treated arm (HR: 0.92; 95% CI 0.71-1.20; p=0.56) and ORR was 15.3% and 14.7%, respectively.
- The median duration of response was 18.6 months for Tecentriq vs. 7.2 months for docetaxel (HR: 0.32; 95% CI: 0.15-0.70). Fifty percent (11/22) of responders had ongoing response in the Tecentriq arm compared with 14% (3/21) in the docetaxel arm.

#### Safety

- At 20 months follow-up, treatment-related Grade 5 and Grade 3-4 adverse events (AE) were experienced in 1% and 12% of Tecentriq-treated patients compared with 2% and 39% of docetaxel-treated patients, respectively.
- Patients who withdrew from treatment due to AE's were 9% in the Tecentriq arm vs. 22% in the docetaxel arm.

Additional data on the use of Tecentriq in non-small cell lung cancer are available.<sup>1-5</sup> Any references supplied to you are protected under U. S. Copyright Law (Title 17, U.S. Code). No further reproduction is permitted.

Respectfully submitted,



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#### Supplemental References

1. Besse B, Johnson ML, Janne PA, et al. Phase II, single-arm trial (BIRCH) of atezolizumab as first-line or subsequent therapy for locally advanced or metastatic PD-L1–selected non-small cell lung cancer (NSCLC). Presented at the European Society for Medical Oncology in Vienna, Austria; September 25–29, 2015. ESMO Oral presentation.
2. Spigel DR, Chaft JE, Gettinger SN, et al. Clinical activity and safety from a Phase II study (FIR) of atezolizumab (anti-PDL1) in PD-L1–selected patients with non-small cell lung cancer (NSCLC). Presented at the American Society of Clinical Oncology 2015 Annual Meeting in Chicago, Illinois; May 29–June 2, 2015. ASCO Poster #8028.
3. Horn L, Spigel DR, Gettinger SN, et al. Clinical activity, safety and predictive biomarkers of the engineered antibody atezolizumab (MPDL3280A, anti-PDL1) in non-small cell lung cancer (NSCLC): update from a Phase Ia study. Presented at the American Society of Clinical Oncology 2015 Annual Meeting in Chicago, Illinois; May 29–June 2, 2015. ASCO Poster #8029.
4. Camidge DR, Liu SV, Powderly J, et al. Atezolizumab (MPDL3280A) combined with platinum-based chemotherapy in non-small cell lung cancer (NSCLC): a Phase Ib safety and efficacy update. Presented at the 16th World Conference on Lung Cancer in Denver, CO; September 6–9, 2015. WCLC Oral presentation.
5. Giaccone G, Camidge DR, Liu SV, et al. Safety, activity and biomarkers of atezolizumab (MPDL3280A) with platinum-based chemotherapy in non-small cell lung cancer (NSCLC): a Phase Ib study. Presented at the European Society for Medical Oncology in Vienna, Austria; September 25–29, 2015. ESMO Poster #P247.

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