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

On behalf of Genentech, I respectfully request the NCCN NSCLC Guideline Panel to consider the enclosed recent publication of the Phase III OAK trial for Tecentriq® (atezolizumab) in patients with metastatic NSCLC.

> Rittmeyer A, Barlesi F, Waterkamp D, et al, for the OAK Study Group. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomized controlled trial. Lancet. E-pub Date: [published online ahead of print] 2016. DOI # 10.1016/S0140-6736(16)32517-X.

Specific Changes:

- For the NSCLC clinical practice guidelines, please consider the addition of the OAK full publication in your updating process.
- For the NSCLC Evidence Blocks™, please also consider updating the Tecentriq Efficacy rating to 4 based on the Phase III OAK full publication, which showed a significant overall survival (OS) benefit in patients treated with Tecentriq compared to those treated with docetaxel (NCCN Evidence Blocks™ Efficacy rating of 3).

FDA Clearance:

Tecentriq is FDA-approved for patients with metastatic non-small cell lung cancer who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Tecentriq.

Tecentriq is also FDA-approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma who received prior platinum chemotherapy. This indication is under accelerated approval based on tumor response rate and duration of response.

Please refer to the Tecentriq prescribing information for the full FDA-approved indication and safety information. http://www.gene.com/download/pdf/tecentriq_prescribing.pdf

Rationale:

Efficacy and safety results from the OAK oral presentation at the European Society for Medical Oncology (ESMO) 2016 Congress were previously submitted.[1] The following summary is based on the recent full publication.

OAK is a Phase III, global, multicenter, open-label, randomized, controlled study conducted to evaluate the efficacy and safety of Tecentriq compared with docetaxel in 1225 patients with locally advanced or metastatic NSCLC whose disease has progressed on or after treatment with platinum-containing chemotherapy. The primary analysis population consists of the first 850 enrolled patients.

Efficacy:

- Compared with docetaxel, Tecentriq demonstrated a clinically and statistically superior 4.2 month OS benefit in the intent-to-treat (ITT) population and 5.4 month OS benefit in the PD-L1 selected patient population (≥1% PD-L1 TC [tumor cell] or IC [tumor-infiltrating immune cell]).

- The following table summarizes primary and key secondary endpoints from the primary analysis (data cutoff July 7, 2016):

Efficacy Results from OAK (ITT and ≥1% PD-L1)		
	Tecentriq (n=425)	**Docetaxel (n=425)**
Primary endpoint		
Median OS (ITT)*, months	13.8	9.6
	HR 0.73; 95% CI, 0.62-0.87; p=0.0003	
Median OS (≥1% PD-L1 TC or IC)*, months	15.7	10.3
	HR 0.74; 95% CI, 0.58-0.93; p=0.01	
12-month OS (ITT)	55%	41%
18-month OS (ITT)	40%	27%
Secondary Endpoints		
Median PFS (ITT), months	2.8	4.0
	HR 0.95; 95% CI, 0.82-1.10; p=0.49	
ORR (ITT), %	14%	13%
Median DOR (ITT), months	16.3	6.2
	HR 0.34; 95% CI, 0.21-0.55; p<0.0001	
*Co-primary endpoints Abbreviations: CI=Confidence Interval; DOR=duration of response; HR=hazard ratio; IC=tumor-infiltrating immune cell; ITT=intent-to-treat; ORR=overall response rate; OS=overall survival; PD-L1= programmed death-ligand 1; PFS=progression-free survival; TC=tumor cell		

Safety:

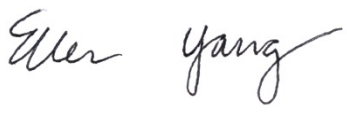
- In the safety-evaluable population (n=1,187), Grade 3-4 adverse events (AEs) were observed in 37% of patients treated with Tecentriq compared with 54% treated with docetaxel. Treatment-related Grade 3-4 AEs were experienced in 15% in the Tecentriq arm compared with 43% in the docetaxel arm.
- In the Tecentriq-treated arm, 8% of patients experienced AEs leading to withdrawal from treatment compared with 19% in the docetaxel arm.
- Grade 3-4 immune-mediated AEs (pneumonitis, hepatitis) for Tecentriq patients occurred in <1%, respectively.

In addition to OAK, Tecentriq also demonstrated a clinically and statistically significant OS benefit of 2.9 months over docetaxel in patients with previously treated NSCLC in the ITT population of the randomized Phase II POPLAR study.[2] Grade 3-4 immune-mediated adverse events that occurred with Tecentriq included increased AST (2%), increased ALT (2%), pneumonitis (<1%), and colitis (1%). Efficacy and safety results from POPLAR were previously submitted.[2,3]

Additional Phase II data on the use of Tecentriq in non-small cell lung cancer are available.[4-6]

 I hope this information is helpful to you. If you have any questions, please contact me directly at (650)-467-0637 or by email at yang.ellen@gene.com

Respectfully submitted,



Supplemental References

1. Barlesi F, Park K, Ciardiello F, et al. Primary analysis from OAK, a randomized Phase III study comparing Atezolizumab with Docetaxel in advanced NSCLC. Presented at the European Society for Medical Oncology in Copenhagen, Denmark; October 7–11, 2016. ESMO Oral Presentation.

2. 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;387:1837-1846.

3. 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; June 3–7, 2016. ASCO Poster #351.

4. 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.

5. Wakelee H, Patel J, Heist R, et al. Phase II trial of atezolizumab for patients with PD-L1–selected advanced NSCLC (BIRCH): updated efficacy and exploratory biomarker results. Presented at the Multidisciplinary Symposium in Thoracic Oncology in Chicago, Illinois; September 22–24, 2016. IASLC Oral presentation.

6. 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.