

**Tumor Board Tuesday – Dr. Narjust Florez (Duma) & Dr. Shruti Rajesh Patel, 09/06/2022:
1st line NSCLC differentiate PD-1/PD-L1 inhibitors**

Posttest Rationale

1. What 1L regimen would you select for a patient with metastatic NSCLC (adenocarcinoma) that is negative for actionable molecular biomarkers and has 54% PD-L1 expression?
 - a. Atezolizumab
 - b. Cemiplimab**
 - c. Nivolumab/ipilimumab
 - d. Pembrolizumab

Rationale: Atezolizumab, cemiplimab, and pembrolizumab are all NCCN guideline-preferred regimen for patients with NSCLC that is PD-L1-positive ($\geq 50\%$) and negative for actionable molecular biomarkers, whereas nivolumab/ipilimumab is considered “useful in certain circumstances” for these patients; all are category 1 recommendations. Cemiplimab is likely the best choice for this patient; when compared to chemotherapy in the phase 3 EMPOWER-Lung01 trial, cemiplimab demonstrated a longer mOS (NR vs 14.2 months; HR 0.57; estimated OS at 2 years: 50% vs 27%), better ORR (39% vs 20%), and longer mPFS (8.2 vs 5.7 months). Pembrolizumab monotherapy may be a good choice for this patient; when compared to chemotherapy in the phase 3 KEYNOTE-024 trial; pembrolizumab has demonstrated prolonged mPFS (10.3 vs 6.0 months) and mOS (NR vs NR; HR 0.60; estimated OS at 6 months: 80.2% vs 72.4%) and improved ORR (44.8% vs 27.8%). Nivolumab/ipilimumab is likely not the best choice for this patient; when compared to chemotherapy in the phase 3 CheckMate 227 trial, nivolumab/ipilimumab demonstrated improved mPFS (6.8 vs 5.0 months), mOS (15.9 vs 10.9 months; HR 0.79), and ORR (38.2% vs 24.9%). Atezolizumab is likely not the best choice for this patient; when compared to chemotherapy in the phase 3 Impower110 trial, atezolizumab demonstrated less robust improvement in mPFS (8.1 vs 5.0 months) and ORR (38.3% vs 28.6%), though mOS (20.2 vs 13.1 months; HR 0.59) was similar to pembrolizumab in the KEYNOTE-024 trial.

References: National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer (v3.2022). Updated March 16, 2022. Accessed April 13, 2022. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

Reck M, Rodriguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. *N Engl J Med*. 2016;375(19):1823-1833. doi:10.1056/NEJMoa1606774

Herbst RS, Giaccone G, de Marinis F, et al. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. *N Engl J Med*. 2020;383(14):1328-1339. doi:10.1056/NEJMoa1917346

Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021;397(10274):592-604. doi:10.1016/s0140-6736(21)00228-2

Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer. *N Engl J Med*. 2019;381(21):2020-2031. doi:10.1056/NEJMoa1910231

2. In what scenario would you opt for systemic rather than continuation maintenance therapy in a patient who received 1L IO for the treatment of metastatic NSCLC?

- a. Complete response
- b. Disease progression**
- c. Partial response
- d. Stable disease

Rationale: The NCCN guidelines recommend systemic therapy (chemotherapy ± IO) for patients who experienced disease progression on a 1L IO regimen.

Reference: National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer (v3.2022). Updated March 16, 2022. Accessed April 13, 2022.

https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

3. What systemic regimen would you select for a patient with metastatic NSCLC who experienced disease progression after 4 cycles of 1L atezolizumab monotherapy?

- a. Atezolizumab + chemo
- b. Chemotherapy**
- c. Nivolumab + chemo
- d. Pembrolizumab + chemo

Rationale: The best choice for this patient is a chemotherapy regimen that does not contain IO. The current NCCN guidelines do not recommend treatment with a PD-1/PD-L1 inhibitor for patients with disease progression on PD-1/PD-L1 inhibitor therapy. This recommendation may change, however, based on results from the Lung-MAP nonmatch substudy S1800A, which demonstrated a statistically significant improvement in overall survival with second-line pembrolizumab plus ramucirumab in patients with advanced NSCLC and immune checkpoint inhibitor resistance compared with standard of care (mOS: 14.5 vs 11.6 months; HR 0.69; 80% CI: 0.51, 0.92), but the combination of pembrolizumab plus ramucirumab is not currently FDA approved.

Reference: National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer (v3.2022). Updated March 16, 2022. Accessed April 13, 2022.

https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

ASCO Daily News. Second-Line Pembrolizumab Plus Ramucirumab Extends OS Over Standard of Care in Advanced NSCLC. Updated June 3, 2022. Accessed September 1, 2022.

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