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. 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

- 2. 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. https://dailynews.ascopubs.org/do/10.1200/ADN.22.200997/full/ 3. Which trial enrolled the greatest percentage of participants with squamous NSCLC, included those with stage 3B and 3C, and excluded never-smokers?

a. EMPOWER-Lung01

- b. KEYNOTE-024
- c. IMpower110

Rationale: EMPOWER-Lung01 enrolled the highest percentage of participants with squamous NSCLC (43.8%), included those with stage 3B and 3C NSCLC, and excluded never-smokers. In the KEYNOTE-024 trial, 18.3% of participants had squamous histology, and in IMpower110, 30.5%.

References: 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