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

Dear Sir or Madam:

On behalf of AstraZeneca, this letter is a formal request to the National Comprehensive Cancer Network (NCCN) Panel for Non-Small Cell Lung Cancer (NSCLC) to review the enclosed data for inclusion of IMFINZI® (durvalumab) as an option for the treatment of locally advanced/metastatic NSCLC with recurrence after at least 2 previous systemic treatment regimens. This request is based on the results of the Phase II ATLANTIC trial published in the *Lancet Oncology* on March 12, 2018 and an updated overall survival (OS) analysis presented at the American Society of Clinical Oncology (ASCO) 2018 meeting.

Specific Change: We respectfully request the addition of durvalumab as an option for patients with NSCLC who have recurrent or progressive disease, wherever appropriate in the guidelines. We have noticed this population is mentioned on pages NSCL-20, NSCL-21, NSCL-22, NSCL-27,

FDA Status:¹

- IMFINZI is not FDA-approved for use in patients for 3rd line or later treatment with Stage III/IV NSCLC.
- IMFINZI 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 duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

- IMFINZI is also indicated for the treatment of patients with unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy

Rationale:

1. The clinical evidence for durvalumab is based on the Phase II (ATLANTIC)², single-arm, open-label, multicenter, international trial in patients with locally advanced or metastatic NSCLC who have received at least 2 prior systemic treatment regimens, including 1 platinum-based chemotherapy regimen. Patients were treated with durvalumab monotherapy 10 mg/kg intravenous (IV) every 2 weeks for up to 12 months and assigned to 1 of 3 cohorts:
 - a. Cohort 1 (n=111): *EGFR*+/*ALK*+, TC \geq 25% and TC<25% PD-L1 expression
 - b. Cohort 2 (n=265): *EGFR*-/*ALK*-, TC \geq 25% and TC<25% PD-L1 expression
 - c. Cohort 3 (n=68): *EGFR*-/*ALK*-, TC \geq 90% PD-L1 expression
2. The primary efficacy endpoint was objective response rate (ORR; complete or partial response) by independent central review per RECIST v1.1. Secondary endpoints included duration of response (DoR), progression free survival (PFS), disease control rate (DCR), overall survival (OS), time to response, and safety.

Efficacy Results

- In Cohort 1 (data cut off date: June 3, 2016), among patients with TC≥25% and EGFR+ only (n=64) the ORR was achieved in 14.1% of patients. The median PFS was 2.0 (95% CI: 1.8-3.7); the 1-year OS was 57.4% (95% CI: 42.8-69.6)²
- In the TC≥25% and ALK+ patient subgroup (n=10) the median PFS was 1.8 months (95% CI: 0.5-1.9). The 1-year OS was 35.7% (95% CI: 9.8-63.3)
- At the latest data cut off (November 7, 2017),³ the median OS for Cohort 1 in high PD-L1 patients was 13.3 months (95% CI: 6.3-24.5), with a 1-year OS rate of 53.3% (95% CI: 40.6-64.4).

Safety Results:

- Treatment-related adverse events (AEs) occurred in 256 (58%) of 444 patients.
 - The most common treatment-related AEs included fatigue (n=50, 11%), hypothyroidism (n=36, 8%), asthenia (n=31, 7%), nausea (n=28, 6%), pruritus (n=28, 6%), diarrhea (n=27, 6%), pyrexia (n=26, 6%), hyperthyroidism (n=24, 5%), and decreased appetite (n=24, 5%).²
 - Forty (9.0%) of 444 patients experienced a grade 3 or 4 treatment-related AE. The most common were pneumonitis (n=4, 1%), elevated gamma-glutamyl transferase (n=4, 1%), diarrhea (n=3, 1%), infusion-related reaction (n=3, 1%), elevated aspartate aminotransferase (n=2, <1%), elevated transaminases (n=2, <1%), vomiting (n=2, <1%), and fatigue (n=2, <1%).²
 - The updated safety analysis was consistent with the previously reported data.³

The following references are submitted in support of this proposal and to assist in your review.

- Garassino MC, Cho BC, Kim JH, et al. Durvalumab as third-line or later treatment for advanced non-small-cell lung cancer (ATLANTIC): an open-label, single-arm, phase 2 study [article and supplementary appendix]. *Lancet Oncol.* 2018;19(4):521-536.
- Garassino MC, Cho BC, Kim JH, et al. Durvalumab in ≥3rd-line advanced NSCLC: Updated results from the phase 2 ATLANTIC study. Presented at ASCO. June 1-5, 2018; Chicago, IL.

Sincerely,

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Reference(s):

- ¹ IMFINZI® (durvalumab) Prescribing Information.
- ² Garassino MC, Cho BC, Kim JH, et al. Durvalumab as third-line or later treatment for advanced non-small-cell lung cancer (ATLANTIC): an open-label, single-arm, phase 2 study [article and supplementary appendix]. *Lancet Oncol.* 2018;19(4):521-536.
- ³ Garassino MC, Cho BC, Kim JH, et al. Durvalumab in ≥3rd-line advanced NSCLC: Updated results from the phase 2 ATLANTIC study. Presented at ASCO. June 1-5, 2018; Chicago, IL