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Date of Request:	June 03, 2019
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 IMFINZI® (durvalumab). This request is based on the updated survival results of the Phase III PACIFIC trial presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting on June 02, 2019.

Specific Change: We respectfully request that the recommendation for IMFINZI (durvalumab) as initial treatment for Stage III inoperable NSCLC following definitive concurrent chemoradiation therapy continue to be supported as category 1 (pages NSCL-2, NSCL-5, NSCL-6, NSCL-8, NSCL-11, NSCL-12). We would like to submit the updated overall survival results based on the follow-up exploratory 36-month survival analysis of the PACIFIC study presented at ASCO as additional support for the current category 1 designation for IMFINZI.

FDA Status:¹

- IMFINZI is 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
- IMFINZI is also 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

Rationale:

1. The PACIFIC study is a Phase III, randomized, double-blind, placebo-controlled, multicenter study in patients with Stage III locally-advanced, unresectable NSCLC who did not have disease progression after at least 2 cycles of platinum-based chemoradiotherapy within 1-42 days prior to randomization.² Patients were randomized 2:1 to receive durvalumab 10 mg/kg IV every 2 weeks (n=476) or placebo (n=237). The primary efficacy endpoints were PFS (according to RECIST v 1.1) per blinded independent central review (BICR) and overall survival (OS).

Primary Efficacy Results:

- As of January 31, 2019, the median duration of follow-up was 33.3 months (range, 0.2-51.3).³
- In this follow-up exploratory 36-month survival analysis, median OS in the durvalumab arm was not yet reached (95% CI, 38.4-NR) compared with 29.1 months (95% CI, 22.1-35.1) in the placebo arm, stratified HR 0.69 (95% CI, 0.55-0.86).³
- As of the final 24-month OS analysis on March 22, 2018, median OS in the durvalumab arm (not reached [NR]; 95% CI, 34.7-NR) was significantly longer compared to the placebo group (28.7 months; 95% CI, 22.9-NR; stratified HR 0.68 (99.73% CI, 0.47-0.997; p=0.0025).⁴

Safety Results:

- As of January 31, 2019, a total of 15.4% of patients in the durvalumab arm and 9.7% of patients in the placebo arm discontinued treatment due to any adverse reactions. No new safety signals were identified and no other safety and tolerability information for durvalumab was reported for the three-year overall survival update.³
- Additional safety and tolerability information was reported and submitted to the NCCN on September 25, 2018.

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

- Gray JE, Villegas A, Daniel D, et al. Three-year overall survival update from the PACIFIC trial [poster]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; June 02, 2019; Chicago, Illinois.
- IMFINZI® (durvalumab) Prescribing Information.

Sincerely,

Asud Khaliq

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Reference(s):

- ¹ IMFINZI® (durvalumab) Prescribing Information.
- ² Antonia S, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage III non-small cell lung cancer. *N Engl J Med*. 2017;377:1919-1929.
- ³ Gray JE, Villegas A, Daniel D, et al. Three-year overall survival update from the PACIFIC trial [poster]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; June 02, 2019; Chicago, Illinois.
- ⁴ Antonia SJ, Villegas A, Daniel D, et al. Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. *N Engl J Med*. 2018;379(24):2342-2350.