7-DAY IND SAFETY REPORT

1. IND NUMBER	2. AGENT NAME	3. DATE
140156	**Pembrolizumab (MK-3475)**	**March 24, 2021**

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION	6. PHONE NUMBER
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8a. PROTOCOL NUMBER (AE #)	8b. AE GRADE: AE
EA5163 (AE # 2446105)	**Grade 5: Lung infection**

9. PATIENT IDENTIFICATION	10. AGE	11. SEX
35257	**49 years**	**Male**

12. PROTOCOL SPECIFIED

Induction: Pembrolizumab + Pemetrexed + Carboplatin: AUC 5
Maintenance: Pembrolizumab + Pemetrexed

13. TREATMENT RECEIVED AND DATES

The patient began the investigational therapy on January 21, 2021, and received the first and only doses of pembrolizumab, pemetrexed, and carboplatin that same day (Cycle 1, Day 1).

14. DESCRIPTION OF ADVERSE EVENT

The patient was a 49-year-old male with metastatic non-small cell lung cancer, who expired on March 1, 2021, from a lung infection while on a Phase III trial utilizing the investigational agent pembrolizumab, in combination with pemetrexed and carboplatin. The patient had a history of anemia of chronic disease and smoking. Of note, the patient underwent thoracentesis with left side pleural catheter placement on November 18, 2020. The patient was hospitalized from January 27, 2021, to January 30, 2021, for diffuse abdominal pain and distension. A CT scan of the abdomen and pelvis showed atelectasis and cystic bronchiectasis in the left lung base, left sided pleural effusion, and distended small bowel loops. He was started on antibiotics for pneumonia and treated with enema and laxatives. On February 15, 2021, he was re-admitted for acute hypoxic respiratory failure along with possible sepsis and was started on antibiotics. A chest CT scan showed extensive changes related to the neoplasm as well as ongoing right pleural effusion and small loculated left pleural effusion. A pleural catheter was recommended, but the patient declined it. A COVID-19 test was negative. On February 17, 2021, he was discharged home with a plan to follow up with his family doctor within a week. On February 22, 2021, the patient presented to the emergency department (ED) with worsening shortness of breath, fatigue, anorexia, poor appetite, and failure to thrive. He had a blood pressure of 108/70 mmHg, a heart rate of 127 beats per minute, a respiratory rate of 36 breaths per minute, a temperature of 98.1°F, and an SpO_2 of 94% on room air. His laboratory results were remarkable for a white blood cell count of 19.38 K/µL (reference range: 4.00 – 11.00 K/µL), a red blood cell count of 3.51 M/µL (reference range: 4.20 – 5.90 M/µL), a hemoglobin level of 10.6 g/dL (reference range: 13.5 – 18.0 g/dL), a hematocrit of 32.6% (reference range 40.0 – 54.0%), and a creatinine level of 0.41 mg/dL (reference range: 0.50 – 1.20 mg/dL). A chest CT scan with contrast showed worsening infiltrates on the right and worsening consolidation/atelectasis in the left lower lobe; bilateral pleural effusions, greater on the right which had increased since prior study; and no evidence of pulmonary embolism. A repeat COVID-19 test was negative. Cultures were obtained, the results of which were not provided; the patient

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was started on broad-spectrum antibiotics. On February 23, 2021, he was started on peripheral parenteral nutrition. He had persistent tachypnea, and an arterial blood gas analysis showed hypoxia of 62.5%. Throughout the day, his oxygen demand had increased from 2 L to 5 L of oxygen via nasal cannula. On February 25, 2021, per the treating oncologist's assessment, the patient was not a candidate for further treatment and comfort care was recommended. On March 1, 2021, the patient expired. An autopsy was not performed. Additional information has been requested from the investigational site.

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using pembrolizumab under NSC 776864= 5,030.

Lung infection is an expected event for pembrolizumab.

16. ASSESSMENT

Based on the provided medical documentation and our medical and scientific knowledge, a possible relationship exists between the lung infection and the investigational agent pembrolizumab.

	Lung infection
Pembrolizumab	**Possible**
Carboplatin	**Possible**
Pemetrexed	**Possible**
Non-small cell lung cancer	**Possible**
Dehydration	**Possible**

17. CONCOMITANT MEDICATIONS

Medications taken at the time of the event were folic acid, lorazepam, metoprolol, oxycodone, and polyethylene glycol.

18. COMMENTS

DISCLAIMER per 21 CFR 312.32(e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB MEDICAL OFFICER/SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.