15-DAY IND SAFETY REPORT

1. IND NUMBER	2. AGENT NAME	3. DATE
125586	**Nivolumab**	**February 10, 2022**

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
9673 (AE #2736950)	**Grade 3: Renal and urinary disorders: Minimal change disease nephrotic syndrome**

9. PATIENT IDENTIFICATION	10. AGE	11. SEX
TX035-134	**71 years**	**Female**

12. PROTOCOL SPECIFIED

Nivolumab

13. TREATMENT RECEIVED AND DATES

The patient began the investigational therapy on August 6, 2021, and received the last dose of nivolumab on October 6, 2021.

14. DESCRIPTION OF ADVERSE EVENT

The patient is a 71-year-old female with metastatic squamous cell carcinoma of the anus who developed grade 3 minimal change disease nephrotic syndrome while on a Phase II trial utilizing the investigational agent nivolumab. She has a history of arthritis, bladder cancer, depressive disorder, neuropathy, suicide attempt, and urinary incontinence, and is a former smoker. On November 5, 2021, the patient presented to the emergency department (ED) with complaints of increased swelling of her legs for the prior 2 weeks and abdominal swelling over the prior 1-2 days. She had a temperature of 98.2°F, a blood pressure of 156/84 mmHg, a heart rate of 92 beats per minute, a respiratory rate of 17 breaths per minute, and an oxygen saturation (SpO_2) of 97% on room air. A physical exam revealed generalized edema and abdominal distension. Laboratory results revealed a creatinine level of 1.54 mg/dL, an albumin level of 2.1 gm/dL, and an alkaline phosphatase level of 137 U/L (reference ranges: not provided). A chest X-ray showed small bilateral pleural effusions. An ultrasound of the liver showed no ascites and a few scattered liver cysts. A venous doppler ultrasound of the legs showed bilateral lower extremity edema but no evidence of deep vein thrombosis. The patient was started on IV furosemide, admitted to the in-patient unit for further management, and monitored for strict water intake and output. On November 7, 2021, a urinalysis revealed proteinuria. A renal ultrasound showed no evidence of a renal mass, hydronephrosis, or nephrolithiasis. On November 8, 2021, following a nephrology consult, the dosage of furosemide was increased, and the patient was planned for a kidney biopsy. On November 9, 2021, an echocardiogram showed normal ejection fraction, no diastolic dysfunction, and no evidence of heart failure. On November 11, 2021, a right kidney biopsy was done which showed minimal change disease, acute tubular epithelial injury consistent with acute tubular necrosis, and 10% interstitial fibrosis with tubular atrophy. On November 12, 2021, the patient was started on prednisone for nephrotic syndrome. On November 13, 2021, the study treatment with nivolumab was held. On November 16, 2021, laboratory results revealed a creatinine level of 1.92 mg/dL. The patient was started on rituximab and a tapering dose of prednisone. On November 19, 2021, she reported an improvement in her symptoms. Physical examination revealed a soft non-tender, non-distended abdomen, and no peripheral edema. Laboratory results showed a drop in creatinine level to 1.54 mg/dL. That day, the

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patient was discharged home in stable condition. Additional information has been requested from the investigational site.

15. ACCRUAL AFND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using nivolumab under NSC 748726 = 8,821. There have been no other cases of minimal change disease nephrotic syndrome reported to the NCI through CTEP-AERS as serious adverse events for nivolumab under NSC 748726.

16. ASSESSMENT

Based on the provided medical documentation and our medical and scientific knowledge, a probable relationship exists between the minimal change disease nephrotic syndrome and the investigational agent nivolumab.

	Minimal change disease nephrotic syndrome
Nivolumab	**Probable**
Squamous cell carcinoma of the anus	**Possible**

17. CONCOMITANT MEDICATIONS

Medications taken at the time of the event were alprazolam, armodafinil, cyanocobalamin, diphenoxylate-atropine, ipratropium nasal spray, loperamide, meloxicam, multivitamin, ondansetron, pregabalin, prochlorperazine, silver sulfadiazine 1% cream, temazepam, bupropion, and desvenlafaxine.

18. COMMENTS