Nivolumab and ipilimumab therapy in a patient with non-small cell lung cancer with chronic kidney disease

Hiroaki Satoh, Sou Hattori

Mito Medical Centre, University of Tsukuba, Japan

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Dear Editor,

Platinum anticancer agents have been key drugs in the treatment of non-small cell lung cancer (NSCLC) without the driver mutation gene. However, they are problematic for some patients with comorbid diseases, especially those with chronic kidney disease (CKD) [1]. With the advent of immune checkpoint inhibitors (ICIs) in recent years, the outcome of treatment for NSCLC has made rapid progress. In particular, the tail plateau of the prognostic curve in combination with nivolumab and ipilimumab and platinum-containing chemotherapy (NIVO/IPI/Chemo) is a surprising result suggesting the possibility of healing [2], and it is a very attractive treatment method for chest physicians. However, the administration of NIVO/IPI/Chemo for patients with CKD must be tentative. We present herein a patient with CKD, who was successfully treated with nivolumab and ipilimumab (NIVO/IPI) therapy.

A recurrence was detected in a 74-year-old man in a follow-up computed tomography scan. FDG-PET revealed a mass in the right lung and pleural dissemination. Eighteen months previously, the patient had received a lobectomy of the right upper lobe of the lung and mediastinal lymph node dissection due to lung adenocarcinoma T1bN0M0. No driver gene was found in the resected specimen, but PD-L1 tumour proportion score was 75%. Laboratory testing revealed blood urea nitrogen (BUN) 22.0 mg/dl and serum creatinine (Cre) 1.22 mg/dl, and eGFR: 45 ml/min/1.73 m^2. Peripheral white blood cell was 7400 mm^3 with peripheral blood eosinophils (PBEs) 3.4%. His physical examination was unremarkable and his performance status (PS, ECOG) was 0. Taking his impaired renal condition into consideration, NIVO/IPI therapy without platinum was selected. The actual dosing schedule was nivolumab (360 mg/body, q – 3 weeks) and ipilimumab (1 mg/kg, q – 6 weeks) therapy. The initial doses of NIVO/IPI were not reduced, and no further dose reduction was required for subsequent ICI administrations. The patient achieved a complete response after the second cycle of this therapy. His BUN fluctuated between 16 and 33 mg/dl, Cre was 1.14–1.46 mg/dl, and eGFR 36–49 ml/min/1.73 m^2, with no exacerbations. He had grade 2 Itchy, but controlled. One year after the start of treatment, he has no recurrence and PS 0 and is fine. In this patient, PBEs were normal before treatment, but PBEs were continuously ≥ 5% on each measurement at the of IPI/NIVO administration. In studies examining the characteristics of patients with NSCLC who responded long-term to ICIs treatment, we reported that patients with PBEs of 5% or higher might have a long-term response [3, 4]. The results were similar with ICIs alone and with chemotherapy [3, 4]. Patients receiving NIVO/IPI were not included in these studies, but these findings suggest that this patient might have a long-term response.

Every combination of ICIs with chemotherapy includes platinum, which is a key drug in chemotherapy for NSCLC patients. This setting of regimens is same in the combination of NIVO/IPI with chemotherapy. Even if carboplatin is used rather than cisplatin, renal toxicities are reported [5, 6]. Chemotherapy in patients with renal dysfunction has been reported to cause early onset and prolongation of myelosuppression [7]. In addition, immune-related adverse events (irAEs) to renal function can occur [8–10], although they are less common. Irreversible renal irAE had also been reported [9]. Another option might be to reduce the dose of platinum, but there has been no established method for determining the appropriate dose. Due to these situations, we sometimes encounter difficulty in the selection of therapeutic drugs for NSCLC patients with CKD. Considering the possibility that the irreversible renal irAEs might increase, the combined use of platinum was not performed in this patient.

Although NSCLC patients with CKD are not uncommon, no standard therapeutic method for these patients has been established. Although careful attention should be paid to renal irAEs as well as non-renal irAEs, clinical information in the present patient suggested that NIVO/IPI is one of the treatment options for NSCLC patients with CKD. It is considered that the treatment experience of this patient will be useful for the treatment of patients with a similar course in the future.

The author declares no conflict of interest.

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Address for correspondence

Prof. **Hiroaki Satoh**
Mito Medical Centre
University of Tsukuba
Tsukuba, Japan
Phone: + 81 29 231 2371
e-mail: hirosato@md.tsukuba.ac.jp

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