Dear Editor,

Immune checkpoint inhibition therapy using targeted monoclonal antibodies is a relatively new therapeutic approach for patients with several cancer types, including non-small cell lung cancer (1). Targeted monoclonal antibodies-based drugs can activate anti-tumor immunity by blocking immune checkpoint receptors (CTLA-4, PD-1 receptor and its ligand PD-L1), in order to restore T-cell effector function (2,3).

Immune checkpoint inhibitor-induced intestinal pseudo-obstruction is a rare but well-recognized adverse effect occurring in approximately 0.5% of patients treated with immune checkpoint inhibitors (1). The pathogenesis of intestinal pseudo-obstruction associated with immune checkpoint inhibitors is not fully understood, and no specific treatment guidelines have been established.

Infliximab, a monoclonal antibody against tumor necrosis factor alpha, has been used for the treatment of immune checkpoint inhibitor-induced intestinal pseudo-obstruction. In a case report, a patient treated with nivolumab for lung adenocarcinoma developed intestinal pseudo-obstruction, which was treated successfully with infliximab (1).

In conclusion, infliximab may be considered as a potential therapeutic option for the treatment of steroid-refractory immune checkpoint inhibitor-induced intestinal pseudo-obstruction.

References:
However, the use of immune checkpoint inhibitors can lead to a unique side effect profile termed immune-related adverse events (irAEs). Loss of T-cell inhibition results in an enhanced immune response driven by T-cell activation and is capable of inducing an autoimmune-related inflammation in normal tissue as a consequence of impaired self-tolerance (4). These irAEs can potentially involve every organ system including gastrointestinal, dermatologic, hepatic and endocrine toxicities. For example, Fernández-Gordón Sánchez et al. reported a patient with immune-mediated colitis and nonimmune-mediated cholestatic injury induced by pembrolizumab that was successfully treated with ustekinumab (5). We report a steroid-refractory case of lung adenocarcinoma in a patient with an unusual irAE (intestinal pseudo-obstruction) during treatment with immune checkpoint inhibitors that was successfully managed by the administration of infliximab.

**Case report**

A 56-year-old male with recurrent lung adenocarcinoma treated with nivolumab was admitted to our hospital with abdominal pain, distension and vomiting for the last two weeks. He had received six cycles of nivolumab at 3 mg/kg every two weeks with the last dose administered four days before the onset of symptoms. Clinical examination revealed a moderate abdominal distension, painful to palpation, without signs of peritoneal irritation and low back pain. His temperature was normal. Subsequent laboratory findings were as follows: white blood cells (WBC) 10.08 x 10^9/l, C-reactive protein (CRP) 26.5 mg/l, albumin (ALB) 24.8 g/l and hemoglobin (Hb) 87 g/l. The abdominal contrast-enhanced computed tomography (CT) revealed bowel distention (Fig. 1). The patient received had a nasogastric tube fitted, with bowel rest treatment with intravenous fluid hydration. After four days of conservative management with no improvement, the patient’s state deteriorated and the small bowel was significantly distended. There were no signs of metastatic disease including lymphadenopathy. After a thorough investigation and exclusion of other factors, suspicion was raised towards the adverse effect of the immune checkpoint inhibition therapy in this patient. Subsequently, steroid treatment (intravenous prednisone 2 mg/kg/day) was initiated, but the patient’s condition did
not improve after high-dose steroid. After infliximab was added, the clinical manifestations and imaging were significantly improved. He continues with immunotherapy, starting two months after discharge. The patient has remained in a stable clinical status during the eight-month follow-up after infliximab therapy and has not presented any similar symptomatology.

References
Fig. 1. A-E. Abdominal computed tomography (CT) showed bowel distention. F. Lung CT showed right lung space-occupying lesions.