Introduction

Lung cancer is the leading cause of death from cancer worldwide [1]. Non-Small Lung Cancer (NSCLC) without driver mutations had limited therapeutic options beyond first line chemotherapy. Based on the current ESMO guidelines Docetaxel is considered as second line therapy in NSCLC without oncogenic driver [2] with an unfavorable safety profile.

Case Report

A 62-year-old male patient was referred to our hospital with persistent cough and unintended weight loss of 10 kilograms within the previous 6 months. The patient was diagnosed with moderate differentiated adenosquamous lung carcinoma, with initial oligometastatic stage IV disease and no driver mutations. After initial treatment with 3 cycles of cisplatin-gemcitabine tumor progression with bone lesions was detected. On immunohistochemistry, the tumor showed a strong (over 50%) expression of PD-L1 on the membrane of tumor cells and treatment with nivolumab was given to the patient. Within two courses of nivolumab the clinical symptoms of acute dyspnea and cough occurred. The diagnosis of nivolumab related pneumonitis was found and the patient received treatment with high dose steroids and antibiotics. A PET-CT scan 12 weeks after the onset of the pneumonitis showed a complete remission of pneumonic infiltrates as well as further response of the bone lesions. Oncological decisions of further treatment included radiological and clinical follow-up without any further treatment with nivolumab. To date, 15 months after the last treatment with nivolumab, the patient is still in complete remission. Nivolumab is the new standard of treatment in second line for NSCLC since the approval of FDA and EMA. This case shows not only how to manage an immune response related pneumonitis. In addition the case showed an exceptional response of this tumor to only two courses of nivolumab.
supraclavicular lymph nodes and local recurrence (Figure 1c). Second line treatment with nivolumab with 3mg/kg every 14 days was initiated. The patient received two courses of treatment and then presented to the emergency unit with dyspnea and cough. The patient’s ECOG performance status was 3, his saturation of Peripheral Oxygen (PiO₂) was 67% without fever and with normal blood pressure values and heart rate. The laboratory findings showed an increase in the LDH with 680 U/l and CRP with 157 mg/l. A CT scan of the thorax showed ground glass opacities in both lungs (Figure 3). Lymph nodes were documented enlarged and anivolumab-induced pneumonitis was suspected as well as tumor progression was considered in differential diagnosis. The patient was treated with high dose steroids methyl prednisolone (MPDN) 250mg iv (single dose) as well as intravenous broad-spectrum antibiotics (piperacillin/tazobactam) for 6 days and switched to oral antibiotics (amoxicillin/clavulanate) for additional 3 days as well as trimethoprim-sulfamethoxazol for a total duration of 15 days. After 3 days from initial treatment, the patients’ conditions improved dramatically with normalization of PiO₂. Corticosteroids were then administered orally and tapered continuously for a total of three weeks (treatment schedule: PDN 200mg for 2days, 100mg for 2days, 50mg for 2days, 25mg for 2days, 20mg for 2days, 10mg for 2days, 5mg for 2days). A PET-CT scan 12 weeks after the onset of the pneumonitis showed a complete remission of pneumonic infiltrates and a metabolic subtotal response and morphological very partial response of the lymph nodes metastases and local recurrence (Figure 1d) as well as further response of the bone lesions. Oncological decisions of further treatment included radiological and clinical follow-up without any further treatment with nivolumab. To date, 15 months after the last treatment with nivolumab and under surveillance after recovery of the immune therapy induced pneumonitis, the patient is still in complete remission.

Discussion

Nivolumab is the new standard of treatment in second line for NSCLC since the approval of FDA and EMA based on the data from the double-blinded phase III study Checkmate 057 comparing nivolumab versus docetaxel [3]. Overall survival, overall response rates as well as median duration of response were favorable in the nivolumab arm. Moreover, grade 3 to 4 treatment-related adverse events were less frequent in the nivolumab compared to the docetaxel group. Although nivolumab is a drug with a very good tolerability and good to moderate drug safety profile, the knowledge as well as the handling of the side effects are the major challenges with this new class of compounds. Beside known adverse events like fatigue and diarrhea, severe toxicities with immunologic related events may also occur. Here we describe a case of nivolumab-induced pneumonitis, which is known to occur in about 1% of the patients as immune related adverse event (irAE) [4]. Typically these irAEs occur between week 6-8 under treatment with PD-1 medication and may present in different clinical severity [5]. Imaging findings of our patient show typical ground glass opacities and some compact formations, as previously described [6]. Also pneumonia or tumor progression should be ruled out in these cases. However, in our patient neither a bronchoscopy nor a biopsy could be performed due to his critical clinical conditions. As previously reported, immune-related pneumonitis should receive corticosteroids intravenously on
an early phase and then taper of dosage should follow clinical and radiographic improvement [6]. Here we describe our treatment scheme and, as we couldn’t exclude pneumonia, antibiotics were added to the corticosteroids. This case shows not only how to manage an immune response related pneumonitis, but also emphasize the exceptional response of this tumor to only two courses of nivolumab.

**Conflict of Interest Statement**

All authors disclose any actual or potential conflict of interest including any financial, personal or other relationship with other people or organizations that could inappropriately influence this work.

**References**


