

## Antineoplastics/corticosteroids/immunoconjugates

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**Immune related adverse events and COVID-19-infection: 4 case reports**

In a case series involving 74 cancer patients who were prospectively followed due to their high risk of getting the COVID-19 infection (patients identified from a single center in UK; study duration 1 February 2020 to 27 April 2020), four men aged 52–72 years were described who developed COVID-19 infection during treatment with ipilimumab, nivolumab, atezolizumab, unspecified immunoconjugates or unspecified corticosteroids. Additionally, two of these 4 men, developed immune related adverse events rash (1 patient receiving ipilimumab and nivolumab) and pneumonitis (1 patient receiving atezolizumab).

Case 1: The man aged 52-years, who had a history of hypertension, was diagnosed with stage-IV renal cell carcinoma with bone metastasis. Subsequently, he started receiving first line treatment with ipilimumab and nivolumab. After the second cycle, he developed immune related adverse event in the form of severe grade III rash, requiring treatment with unspecified corticosteroids for 28 days. Four days after the completion of corticosteroid therapy, he developed fever, cough, rigor and dyspnoea (3 months after chemotherapy start and 8 weeks after the last chemotherapy dose). Consequently, he self isolated; however, as the condition progressed, he was hospitalised. At the time of admission, his body temperature was 38°C and oxygen saturation was 60%. Laboratory tests showed elevated levels of CRP and ferritin. A chest x-ray showed bilateral lung infiltrates. Subsequently, he was diagnosed with COVID-19 pneumonia, and off label treatment was started with IV amoxicillin/clavulanic-acid [Co-amoxiclav] and clarithromycin. After 48 hours, signs of improvement were noted. After 32 days from the initial onset of symptoms, he was discharged from the hospital with plan to re-initiate the chemotherapy.

Case 2: The man aged 68-years, who had a history of hypertension, was diagnosed with stage-IV renal cell carcinoma with lung metastasis. Subsequently, he started receiving first line treatment with ipilimumab and nivolumab. Three weeks after the chemotherapy initiation and 2 weeks after the last chemotherapy dose, he developed dry cough and fever (body temperature of 38.8°C). A diagnosis of COVID-19 infection was confirmed, and he was placed under self isolation protocol (UK policy). After 5 days, his fever and cough resolved. Chemotherapy was re-started after completion of the self-isolation period.

Case 3: The man aged 66-years, who had a history of hypertension, was diagnosed with stage-IV urothelial carcinoma with lung metastasis. Subsequently, second line chemotherapy was started with atezolizumab. Later, he developed immune related adverse event in the form of pneumonitis confirmed by chest CT. Consequently, chemotherapy was stopped and treatment was started with unspecified corticosteroids. After successful treatment, the corticosteroids were stopped after 28 days of treatment, and chemotherapy was re-initiated. However, 6 months after the chemotherapy initiation (total duration) and 3 weeks after the last chemotherapy dose, he developed cough and dyspnoea with oxygen saturation of 93%. COVID-19 infection was confirmed, and he was placed under self isolation protocol (UK policy). Moderate elevation was noted in his CRP levels. His cough and dyspnoea resolved within 10 and 7 days, respectively. Chemotherapy was re-started 36 days after the initial development of COVID-19 symptoms.

Case 4: The man aged 66-years, who had a history of hypertension and diabetes, was diagnosed with stage-IV urothelial carcinoma with lymph node metastasis. Subsequently, second line chemotherapy was started with atezolizumab. As symptomatic cancer progression was noted, unspecified immunoconjugates [antibody drug conjugate] were added to the treatment. However, 4 months after the chemotherapy initiation and 3 weeks after the last chemotherapy dose, he developed cough and was placed in home quarantine. COVID-19 infection was confirmed. After 2 days, the patient developed diarrhoea, which led to severe dehydration. Ten days after onset of symptoms, he was hospitalised. Laboratory tests showed acute kidney injury with creatinine level of 276 mg/dL, mild CRP elevation and lymphocytopenia. He was started on fluid replacement therapy and off label IV piperacillin/tazobactam. Rapid improvement was noted in his condition. After 48 hours, he was discharged. Thirty one days after the initial onset of COVID-19 symptoms, atezolizumab therapy was re-started.