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Effect of immune checkpoint inhibitors on asthma



Anticancer strategies using immune checkpoint inhibitors (CPIs) are increasingly being used. The most common strategies involve monoclonal antibodies targeting cytotoxic T lymphocyte associated antigen-4, programmed cell death protein (PD-1), and programmed cell death ligand 1.¹ By blocking the natural regulation of T cells, they activate cytotoxic T cells and shift the immune system toward antitumor activity. In some patients, adverse events have been seen with these therapies.¹ Mechanistically, it has been suggested that immune-related adverse events (irAE) may be linked to an autoimmune process secondary to T-cell receptor inhibitory phosphatases that maintain tolerance to autoantigens.²

Pneumonitis has been described as a rare but potentially life-threatening irAE, with a frequency of 5% in patients treated with anti-PD-1 or programmed cell death ligand 1 therapy.² However, exacerbations of preexisting lung conditions have not been ascertained. The study by Galant-Swofford et al³ reported that pneumonitis occurred more frequently in patients with a history of asthma and chronic obstructive pulmonary disease than in those without this history. Despite this, to the best of our knowledge, there have not been any other studies that support this finding.³ Asthma is characterized by the increased presence of T helper 2 cell lymphocytes and eosinophils.³ A recent case report study has described asthma as an irAE in a patient aged 70 years, diagnosed with unresectable bladder cancer on anti-PD-1 therapy.^{4,5} Because of this case study, and the fact that CPIs have been documented to increase eosinophil levels,⁶ we were interested in the relationship between CPIs and asthma, specifically whether CPIs worsen underlying asthma.

Our study is a collaborative project between Memorial Sloan Kettering Cancer Center in New York and National Jewish Health in Denver. As of January 5, 2022, we enrolled 83 patients with grade 2 or higher immune-related cutaneous adverse events (ircAE) and 32 subjects in our comparison group: those on CPIs without any ircAEs. Based on a self-reported atopic diseases questionnaire, 13 patients in

the study have reported a history of asthma. Six of these patients had pruritus without rash; 3 had eczema; 1 had a maculopapular rash; and 3 had no cutaneous adverse events.

Of the 13 patients with a history of asthma, most were White men (11 of 13 White, 9 of 13 male) with an average age of 65 years (ranging from 41 to 87 years old). Four were treated for kidney cancer, 2 for bladder cancer, 2 for thyroid cancer, 1 for prostate cancer, 1 for pancreatic cancer, 1 for endometrium cancer, 1 for liver cancer, and 1 for melanoma. Four had no asthma medications listed; 4 of them were on inhaled corticosteroids (ICS) with short acting bronchodilators as rescue (2 with leukotriene inhibitor as well); 2 were on inhaled corticosteroids and a long-acting bronchodilator (ICS-LABA) with a short acting beta agonist (SABA) as rescue; 1 was on SABA only; 1 was on an oral leukotriene inhibitor only; and 1 was on SABA and an oral leukotriene inhibitor. With the introduction of a CPI, 1 patient had 5 mg prednisone added to their asthma regimen (changing from ICS + SABA + leukotriene inhibitor to ICS + SABA + leukotriene inhibitor + 5 mg prednisone), and another had a leukotriene inhibitor added (ICS + SABA + montelukast). The remaining 11 patients had no change in asthma medications after starting CPIs, including those with no asthma medication listed, even though 9 of 11 of those patients had an increase in eosinophil levels with the increase ranging from 1.4 to $11 \times 10^9/L$; $P = .05$). Thus, although lung adverse events, like pneumonitis, can be induced with CPI use, we found no evidence for exacerbation of asthma in our patient population.

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