

Table SI. Additional respiratory related adverse events and their management strategies.

Author (year)	System	Cancer	irAEs	Drug	Clinical manifestations	Responses	References
Heleno (2021)	Neuro muscul ar system	Undifferen tiated pancreatico biliary adenocarci noma	Myasthenia Gravis (MG)	Pembrolizum ab	/	Taking pyridostigmine, the use of pembrolizumab was discontinued.	(41)
Liu (2021)		Melanoma	Polymyositis with associated spontaneous muscular	Nivolumab	Twenty days after the first infusion of nivolumab, he developed a 7-day history of exertional dyspnea and diplopia. Laboratory tests show that there may be myositis, accompanied	Begin a five-day course of intravenous immunoglobulin (IVIG) at 0.4 g/kg once a day. After IVIG, methotrexate was injected subcutaneously every week with an initial dose of 10	(35)

			hematoma		by myocarditis and rhabdomyolysis	mg, and methylprednisolone was slowly stopped. The patient gradually improved clinically, troponin decreased, and creatine kinase levels returned to normal, but the extubation time was prolonged due to respiratory failure. Three months later, he finally left the intensive care unit. Repeated CT imaging 3 months after admission showed initial resolution of the hematoma	
Moreira (2019)		Metastatic skin cancer	Myositis	Ipilimumab, tremelimumab, nivolumab	Myositis is the most common neuromuscular adverse event. In 32% of cases, myositis is complicated by	For patients, the occurrence of these side effects must be considered, especially when	(94)

				and pembrolizumab	myocarditis. In addition, cases of isolated myocarditis, myasthenia gravis, polymyalgia rheumatica, radiculopathy, and asymptomatic elevated creatine kinase have been reported.	considering the use of anti-programmed cell death protein 1 (PD-1) antibodies for adjuvant immunotherapy and monitoring, which should include regular monitoring of creatine kinase.	
Makarios (2017)		Metastatic melanoma	Pembrolizumab-induced MG	Pembrolizumab	An 85-year-old woman with metastatic melanoma with enlarged left axillary lymph nodes started pembrolizumab monotherapy (2 mg/kg; every 3 weeks) and tolerated the first cycle without any significant toxicity. Shortly after the second cycle, she developed diplopia, followed by asymmetric bilateral ptosis (L > R).	Given the high clinical suspicion of myasthenia gravis, she started systemic therapy with intravenous injections of immunoglobulin, prednisone, and pyridostigmine. The program caused a rapid clinical response and completely resolved bilateral ptosis and diplopia. She continued to maintain	(36)

						monthly IVIG and daily oral pyridostigmine without any further recurrence of symptoms.	
Parakh (2018)	Respiratory system	NSCLC	Immune checkpoint inhibitor-associated pneumonia	Nivolumab	A 70-year-old man with poorly differentiated squamous cell carcinoma of the lung was diagnosed with immune checkpoint inhibitor-associated pneumonia grade 3 during the second-line single-agent nivolumab after the progression of first-line chemotherapy.	After high-dose glucocorticoid shock therapy, the patient's clinical symptoms were partially relieved, and then oral pirfenidone (300 mg three times daily) was administered for more than 11 months. During the treatment of pirfenidone, the CT images and clinical symptoms of the patient were significantly improved.	(93)

Donato (2019)		Squamous cell carcinoma with lung metastasis to the sacrum and liver	Allergic bronchopulmonary aspergillosis	Pembrolizumab	A patient with asthma and mild eosinophilia was treated with the PD-1 inhibitor pembrolizumab for 4 months. Aspergillus fumigatus IgG increased to 15.60 U/mL (normal value: <12.01 U/mL).	He responded to treatment with corticosteroids and voriconazole, and was able to recover pembrolizumab with a good clinical response.	(51)
Fragkou (2016)		Nasal mucosal melanoma	Organizing pneumonia	Pembrolizumab	A 64-year-old woman with nasal mucosal melanoma involved the cervical and mediastinal lymph nodes and metastasized to the liver, brain, and bones. After receiving second-line immunotherapy of pembrolizumab, lower respiratory tract infections mainly affect all lung lobes.	Treatment with corticosteroids (prednisolone 50 mg/day, intravenous injection) was started, which led to rapid clinical and radiological improvement in the patient. Three months later, the patient died of late-stage metastatic disease in the brain.	(52)

Vartanov (2021)	Circulatory system	Metastatic NSCLC	III AVB	Combination ipilimumab-nivolumab	The patient started to use ipilimumab and nivolumab in combination 15 days before admission. The lower extremity swelling worsened at the time of admission. The electrocardiogram showed sinus rhythm, left bundle branch block and gradually prolonged PR interval, and the developing heart Consistent conduction block, neutrophil leukocytosis, orthocytic anemia, initial troponin I was 1.36 (laboratory normal value <0.30 ng/mL), on the third day of hospitalization, the patient was found to have cardiac arrest and eventually passed away	Symptomatic treatment	(53)
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Liu (2021)		Melanoma	Impaired cardiac function	Pembrolizumab	Echocardiographic studies have shown that the left ventricular function is severely impaired and accompanied by asynchrony. All tests for cardioviruses were negative. Histological analysis of myocardial biopsy showed lymphocyte infiltration, CD8 positive cells were predominant, and FOXP3 positive regulatory T cells were reduced.	After starting corticosteroids and heart failure treatment in line with guidelines, symptoms improved rapidly and left ventricular function recovered	(35)
Bukamur (2019)		Squamous Cell Lung Carcinoma	Third Degree Atrioventricular Block	Nivolumab	An 88-year-old female patient with a previous history of hypertension and hyperlipidemia taking statins. After completing two cycles of nivolumab (240 mg every two weeks), she suffered from muscle pain and proximal He was admitted to the	An electrophysiologist was consulted, and a temporary transvenous pacemaker was inserted, and then a permanent pacemaker was inserted. The patient's overall condition has improved and she has been	(55)

					hospital due to weakness, stopped statins, and the patient started taking high-dose pulse steroids. An echocardiogram showed increased myocardial thickness without signs of ischemia. During the hospitalization, she developed sinus bradycardia and progressed to complete atrioventricular block	discharged to a professional nursing facility.	
Neilan (2018)		Pan-cancer	ICIs-associated myocarditis	ICIs	In patients receiving ICI treatment, myocarditis has become a rare but potentially life-threatening adverse reaction. The assessment and characterization of ICI-related myocarditis is challenging because of its low incidence and variable manifestations. Nevertheless, the	In the case of confirmed or suspected myocarditis, consult a cardiologist, stop ICI treatment, and use high-dose corticosteroids (for example, 1 mg/kg methylprednisolone)	(95)

					severity of ICI-related myocarditis proves that coordinated efforts are needed to raise awareness of the syndrome, identify patients who may be at risk, and achieve early diagnosis and appropriate treatment		
Alnabulsi, R (2018)		metastatic melanoma	Diffuse panmyositis	Ipilimumab/ Nivoluma	Patients with metastatic melanoma developed fatal and severe diffuse panmyositis after combined treatment with Ipilimumab/Nivolumab, involving the heart, breathing, and extraocular muscles.	/	(96)
Liu (2021)		Metastatic uveal melanoma	Severe heart failure due to autoimmune myocarditis	Pembrolizumab	The echocardiogram showed severely impaired left ventricular function and desynchronization. All tests for cardiotropic viruses were negative.	After starting the use of glucocorticoids and heart failure treatment in accordance with the guidelines, the	(35)

					Histological analysis of myocardial biopsy showed lymphocyte infiltration, CD8 positive cells were predominant, and FOXP3 positive regulatory T cells were reduced.	symptoms improved rapidly and the left ventricular function was restored.	
Kurokawa, M (2021)	Digestive system	Pan-cancer	Enterocolitis	α PD-1-EC	Patients often develop pancolitis, skipping lesions, and appendix involvement		(97)
Luoma (2020)		Pan-cancer	Colon Inflammation	Checkpoint blockade using specific antibodies against PD-1 and CTLA-4 inhibitory	Significant accumulation of CD8 T cells with a high degree of cytotoxicity and proliferation, and no evidence of depletion of regulatory T cells. T cell receptor (TCR) sequence analysis shows that a large proportion of colitis-associated CD8 T cells come from the tissue-resident	Identified cytokines, chemokines, and surface receptors, which can be used as therapeutic targets for colitis, as well as other potential inflammatory side effects of checkpoint blockade.	(98)

				receptors can induce durable responses in a variety of human cancers.	population		
Zhao, L (2020)		/	Diarrhea	ICIs	/	The risk of diarrhea after the combination of PD-1/PD-L1 inhibitors and CTLA-4 inhibitors is significantly higher than that of monotherapy	(99)
Tso (2020)		Metastatic non-small cell lung	Small bowel obstruction	Nivolumab	The patient is receiving nivolumab for long-term treatment of metastatic non-small cell lung cancer. She went	The patient underwent a laparotomy	(58)

		cancer			to the emergency department due to acute abdominal pain. CT showed a small dilated proximal ileum, near a very short intestine, with thickened walls and perforations near the transition point.		
Shivaji (2019)		/	Immune-related colitis and hepatitis	ICIs	/	Early oral steroid intervention is effective for most patients. Infliximab and vedolizumab are reported to be useful for steroid-refractory colitis; mycophenolate mofetil has been used to treat steroid-refractory hepatitis	(100)
Alvarez, M. (2019)		/	Corticosteroid-refractory	ICIs	/	TNF neutralization is used to treat corticosteroid-refractory	(101)

			immune-related adverse events (irAEs)			immune-related adverse events (irAE) caused by anti-PD-1 and anti-CTLA-4 combined immunotherapy. The results of the study prove that preventive TNF neutralization and ICB treatment strategies are successfully combined to improve toxicity while maintaining or even improving anti-tumor efficacy.	
Mathew Thomas (2020)		Recurrent renal cell carcinoma	Hepatitis	Nivolumab	A woman treated for recurrent renal cell carcinoma developed hepatitis. Test results for other reasons are negative, hepatitis is attributed to the use of nivolumab	The patient took steroids and then started to get better. However, she later presented with massive upper gastrointestinal bleeding secondary to gastroduodenal	(59)

						ulcer, then developed acute tubular necrosis and died from complications	
Nadeau, B.A (2018)		/	Hepatotoxicity of checkpoint inhibitors	/	Hepatotoxicity of checkpoint inhibitors is a less common irAE, usually mild, and its incidence and severity vary with the type and dose of checkpoint inhibitors, monotherapy and combination therapy, and cancer type.	Liver irAE may need to stop checkpoint inhibitor therapy and immunosuppressive therapy.	(102)
Straub (2018)		/	Liver damage	ICIs	In all 9 patients, liver damage was obvious after the administration of immune checkpoint inhibitors to varying degrees. The level of transaminase increased to a maximum of 3818 U/l. Liver	In all 9 patients, liver damage was obvious after the administration of immune checkpoint inhibitors to varying degrees. The level of transaminase increased to a	(103)

					histology shows that liver damage is similar to the cholangitis of autoimmune hepatitis. In two patients, venous occlusive disease was found.	maximum of 3818 U/l. Liver histology shows that liver damage is similar to the cholangitis of autoimmune hepatitis. In two patients, venous occlusive disease was found.	
Lankes (2016)		Metastatic melanoma	Immune-mediated colitis	Ipilimumab	The patient has up to 18 watery stools per day	After immunosuppressive therapy (high-dose steroids and infliximab) combined with parenteral nutrition therapy, the condition improved and then worsened again. Antiviral medication was given while reducing corticosteroids, and symptoms improved. The patient showed complete	(60)

						remission for 2 years, including regression of bone metastases.	
Kichloo (2020)	Endocrine System	Metastatic colon adenocarcinoma	Diabetes and diabetic ketoacidosis	Pembrolizumab	A 77-year-old woman with a history of metastatic colon adenocarcinoma, new-onset diabetes and diabetic ketoacidosis while receiving pembrolizumab chemotherapy	The patient underwent rehydration, insulin therapy and electrolyte management, and was finally discharged from the hospital, requiring home insulin therapy to control her new-onset diabetes	(61)
Rahman, W. (2020)		Metastatic renal cell carcinoma.	Type 1 diabetes	Atezolizumab	Atezolizumab is a checkpoint inhibitor against PD-L1 and is associated with rare complications of type 1 diabetes.	/	(104)
		/	Autoimmune diabetes	/	Immune checkpoint inhibitor-induced diabetes (CPI-DM) is characterized	/	(105)

					by acute onset of severe hyperglycemia and severe insulin deficiency		
Agrawal, L. (2020)		Pan-cancer	Hypothyroidism, hyperthyroidism, diabetes and hypoparathyroidism, hypophysitis	ICPIs	/	/	(106)
Bailly (2019)			Autoimmune thyroiditis	Monoclonal antibodies targeting the immune	Autoimmune thyroiditis (Hashimoto's thyroiditis) is a common side effect observed after treating cancer patients with a monoclonal antibody against immune	EDA can improve autoimmune thyroiditis (Hashimoto's thyroiditis).	(107)

				checkpoint PD-1	checkpoint PD-1		
Zhu, Y (2019)		Advanced small-cell lung cancer	Hypophysitis	Nivolumab	Reported a case of corticotropin deficiency during treatment of advanced small cell lung cancer, which may be caused by nivolumab-induced hypophysitis.	Symptomatic treatment for hypophysitis and related symptoms	(108)
Li (2018)		NSCLS	Autoimmune diabetes and diabetic ketoacidosis	Pembrolizumab	Excessive thirst, polyuria, weakness and weight loss after treatment with anti-programmed cell death-1 antibody. Hyperglycemia, high serum ketones, low bicarbonate and high anion gap meet the diagnostic criteria of diabetic ketoacidosis (DKA).	The patient stopped taking pembrolizumab and started continuous subcutaneous insulin infusion (CSII) at the same time. Change the insulin infusion to multiple daily injections (MDI) after discharge	(109)

Solinas (2018)		/	Immune-related hypophysitis	ICI	Patients may have headaches, visual disturbances, or other endocrine-related symptoms, or they may be asymptomatic. The manifestation of symptoms should prompt blood analysis and brain magnetic resonance imaging. Imaging examination is very important to rule out secondary meningeal or parenchymal lesions	Management should include stopping immune checkpoint blockade, initiating corticosteroid therapy, and finally hormone replacement therapy.	(110)
Briet (2018)		/	Hypophysitis	/	Unclear clinical symptoms (usually headache and fatigue) and/or hyponatremia and/or at least one pituitary gland defect and/or imaging abnormalities. Visual disturbances or polymorphic frequently-occurring syndromes are exceptions.	The treatment of corticotropin deficiency requires systematic emergency replacement therapy. Thyroid stimulating hormone and gonadotropin deficiency can usually be restored, but corticotropin	(111)

						deficiency is long-term and requires education and special endocrine follow-up. The onset of hypophysitis is not contraindicated to continue immunotherapy, and high-dose synthetic glucocorticoids are usually not required.	
Clotman, K. (2018)		/	Diabetic ketoacidosis	Pembrolizumab	/	Blood glucose monitoring is necessary during anti-pd-1 treatment.	(112)
Sagiv (2019)		/	Thyroid eye disease (TED)-like orbital inflammatory syndrome	ICI	The patient was previously diagnosed with Graves disease without TED and developed TED shortly after starting treatment with a programmed cell death protein 1 inhibitor	Systemic steroids or observation therapy, the symptoms are alleviated, and there is no need to stop the immune checkpoint inhibitor	(113)

						treatment for the cancer	
Gauci (2017)		metastatic melanoma	Autoimmune diabetes	Nivolumab	A 73-year-old man received 3 mg/kg nivolumab as second-line treatment for metastatic melanoma every two weeks. During 6 weeks of treatment, he showed diabetic ketoacidosis.	Nivolumab was discontinued for 3.5 weeks and insulin therapy was started to normalize blood sugar and disappear symptoms	(114)
Okamoto (2016)		Melanoma	Insulin dependent diabetes	Anti- programmed cell death-1 therapy	Ketonuria had a sudden onset, and blood sugar (580 mg/dL) and glycosylated hemoglobin (7.0%) increased. In the next two weeks, serum c-peptide levels fell below the detection limit. Pancreatic islet autoantibodies were negative, and the patient showed a haplotype of human leukocyte antigen associated with type 1 diabetes.	Treatment for diabetes	(115)

Rossi (2016)		NSCLC	Endocrinopathies	Nivolumab and pembrolizumab	The use of nivolumab and pembrolizumab can cause a series of endocrine disorders	/	(116)
Kim, K.H. (2021)	Skin lesions	HCC	Alopecia areata	Nivolumab	Histopathology found that the hair follicles were reduced in the transverse section, and lymphocytes infiltrated around the hair follicles in the longitudinal section.	Patients with topical steroids and minoxidil, symptoms relieved	(117)
Navarro-Fernandez (2021)		Melanoma/ Metastatic RCC	Vitiligo-like depigmentation (VLD)	Nivolumab	Inhibition of PD-1 may lead to loss of tolerance to melanocyte antigens, leading to CD-8 T cell dependent destruction of melanocytes present in melanoma and healthy skin	Protect colorless areas from sunlight	(118)
Mullangi		Renal cell carcinoma	Psoriasis	Nivolumab	Palmar and plantar involvement	He started using triamcinolone topical steroids, which did not	(65)

(2021)						help his symptoms, and he needed apres and retinoids. Nivolumab continued to be used. Three months later, he developed severe diarrhea and required systemic steroids and infliximab. At the last follow-up two years after stopping nivolumab, the symptoms did not recur.	
Acar, A. (2021)		Melanoma	Plaque morphea	Nivolumab	Plaque and hard plaque lesions appeared during nivolumab treatment, but there was no systemic involvement	Plaque lesions respond well to topical corticosteroids and calcipotriol	(66)
Gracia-Cazana		Malignant melanoma	Vitiligo-like lesions	Pembrolizumab	A patient with melanoma started treatment with pembrolizumab	/	(119)

(2019)					2mg/kg. During the follow-up, leukoplakia-like lesions appeared in the primary and metastatic areas.		
Mobini (2019)		Metastatic renal cell carcinoma/melanoma	Nodular dermatitis and panniculitis	Ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1)	A 49-year-old woman has a history of renal cell carcinoma, clear cell type. Seven months later, the patient developed metastatic lung disease. She then received treatment with nivolumab (opdivo) and ipilimumab (yervoy). One month after the first round of treatment, the patient developed large, non-tender, hard subcutaneous nodules and plaques on the left forearm and elbow. These nodules and plaques were more obvious than the naked eye. Skin biopsy revealed granulomatous	After consulting with the treating oncologist, it was decided to stop the checkpoint inhibitor treatment after the third round. During the following three weeks of follow-up, the patient reported that the size and hardness of the lesion were decreasing.	(67)

					inflammation of the dermis and subcutaneous tissue. Nodular dermatitis and panniculitis are thought to be secondary to the combination therapy with opdivo and yervoy.		
Cardis (2019)		Merkel cell carcinoma	Diffuse lichen planus-like keratoses	Avelumab	Diffuse lichen planus-like keratoses and clinical pseudo-progression associated with avelumab treatment for Merkel cell carcinoma, a case report.	The appearance of skin symptoms corresponds to an inflammatory cancer response (clinical pseudo-progression), and as the overall tumor burden decreases, the rash improves. Patients with itching are treated with topical steroids and cryotherapy for individual symptomatic lesions.	(120)

De Bock (2018)		Melanoma	Psoriasis exacerbation	Nivolumab	A 65-year-old woman received nivolumab (anti-PD-1) for stage IV melanoma. She has a history of scalp psoriasis, and both lower and upper limbs have psoriasis lesions. The psoriasis worsened during treatment	Our patient received topical steroid therapy.	(68)
Rambhia (2018)		Metastatic melanoma	Inflammation of seborrheic keratosis and new verrucous keratosis	Nivolumab	A patient with metastatic melanoma treated with PD-1 inhibitors subsequently developed existing seborrheic keratosis lesions and new verrucous keratosis inflammation, which is a skin side effect that we have not previously reported	The use of moderately potent topical steroids and cryotherapy has a certain effect on symptomatic lesions.	(121)
Lopez, A.T (2018)		/	Bullous pemphigoid (BP)	PD-1 and PD-L1 inhibitors.	It is reported in the literature that bullae appear within 6-8 months after starting PD-1/PD-L1 inhibitors;	In 76% (16/21) of cases, the development of BP requires discontinuation of	(122)

					pembrolizumab and nivolumab have similar average time to itching at 19 weeks and 21 weeks, respectively.	immunotherapy.	
Obara (2018)		/	Oral lichenoid reaction	Anti-PD-1 antibody	Both patients presented with multiple ulcers covering the entire oral mucosa, lips, and tongue with fibrin plaques. Histopathological examination of the ulcer showed epithelial necrosis and sub-epidermal fissures, and dense band-like lymphoid tissue cell infiltration in the upper dermis	Case 1 has a good local corticosteroid response. Case 2 requires oral glucocorticoids	(123)
Schneider (2021)	Urinary system	Melanoma	Aseptic cystitis	Nivolumab and ipilimumab	After two infusions, diarrhea, frequent urination, severe bladder pain, urgency and nocturia	Oral steroids seem to be the most effective treatment option.	(71)
Seethapathy		Pan-cancer	AKI	Programmed	Although AKI is common in patients	/	(124)

(2020)				Cell Death Ligand-1 Inhibitors	receiving PD-L1 treatment, compared with other types of ICI, the incidence of suspected PD-L1-related AKI is low (<1%) and may be less common.		
Thummalapalli, R (2020)		Melanoma	Acute kidney injury	Pembrolizumab	A case of a BRAF mutant melanoma patient who received the initial infusion of anti-PD-1 therapy while taking RAF/MEK inhibitors and experienced severe acute kidney injury.	Corticosteroid therapy quickly reversed this process	(72)
Uchida (2017)		Lung adenocarcinoma	Acute tubulointerstitial nephritis	Nivolumab	A 67-year-old Japanese man with lung adenocarcinoma treated with nivolumab developed acute tubulointerstitial nephritis after the third infusion of nivolumab. Kidney biopsy revealed different histological	Nivolumab was discontinued and oral prednisolone 30 mg was started. Oral prednisone gradually decreased. On day 98, the values of serum creatinine, urine β 2MG, and	(73)

					findings: the proliferation of CD38-positive and IgG-positive plasma cells, and the massive infiltration of FoxP3+ regulatory T cells.	NAG were 2.42, 9.38 mg/dL, and 9.4 U/L, respectively. When recovering from nivolumab-induced tubulointerstitial nephritis, the patient did not receive any treatment for lung cancer.	
Bickel (2016)		Malignant pleural mesothelioma	Acute kidney disease Functional failure	Pembrolizumab	A 62-year-old patient diagnosed with malignant pleural mesothelioma suddenly developed systemic edema, including legs and eyelids, 10 days after receiving the second dose of third-line pembrolizumab. Nephrotic syndrome caused a weight gain of 15 kg, acute kidney disease Functional failure.	The patient immediately stopped pembrolizumab and started using prednisone, diuretics, and angiotensin II receptor blockers. The symptoms and renal function were completely restored.	(125)

Boegeholz (2020)	Blood system	Pan-cancer	Cancer immunotherapy via immune-checkpoint inhibition (ICI)	Neutropenia	The median onset time of neutropenia after the first ICI administration was 10.5 weeks, some of which were fever and infection	The treatment options are correspondingly different, but mainly include G-CSF and intravenous corticosteroids	(126)
Jotatsu, T. (2018)		Non-small cell lung cancer	Nivolumab	Thrombocytopenia after transient mild fever	Fever and C-reactive protein level increased on the 2nd day after the first infusion of nivolumab, the fever subsided on the ninth day, and severe thrombocytopenia appeared on the 15th day.	Taking 60 mg of prednisolone daily can restore the patient's platelet count and platelet-related IgG	(77)
Jotatsu, T. (2018)		Lung cancer	Nivolumab, pembrolizumab, ipilimumab,	Fulminant warm antibody	IgG was detected on red blood cells in some patients, which is consistent with warm autoimmune hemolytic	Receiving steroid treatment	(77)

			atezolizumab	autoimmune hemolytic anemia	anemia		
Obata, S. (2019)	Eye damage	Metastatic skin malignant melanoma	Vogt-Koyanagi-Harada disease (VKH)-like uveitis	Nivolumab	A 63-year-old woman with metastatic skin malignant melanoma developed binocular vision loss 10 days after the second nivolumab injection.	Anterior chamber inflammation disappeared 3 weeks after starting topical corticosteroid treatment	(79)
		Patients with metastatic renal cell carcinoma	Uveitis Grade 4 panuveitis with bilateral serous retinal detachment	Nivolumab	Grade 4 panuveitis with bilateral serous retinal detachment after nivolumab treatment of metastatic renal cell carcinoma	Oral prednisone, topical steroid eye drops, periorbital injection of steroids, and finally intravitreal injection of steroid implants. Oral prednisone is also effective, but may affect the efficacy of anti-PD -1 therapy and promote tumor	(127)

						growth	
Theillac (2017)		Calf melanoma with duodenal and lymph node metastasis	Bilateral anterior uveitis and macular serous retinal detachment	Nivolumab	A man who received nivolumab for leg melanoma with duodenal and lymph node metastases suddenly developed bilateral visual impairment and bilateral non-painful red eyes a few days after the third infusion.	Oral corticosteroid therapy	(80)
Buder-Bakhaya (2018)	Joint damage	Metastatic cutaneous malignancies	Arthralgia	Pembrolizumab or nivolumab + ipilimumab	In most cases, joint pain affects the large joints (shoulder, knee) and is mainly symmetrical. Only 2 patients were seropositive for rheumatoid factor and/or anti-citrulline protein antibodies. Ten patients had clinical manifestations of arthritis, and 7 of them showed synovitis on MRI or	Most patients received non-steroidal anti-inflammatory drugs (NSAIDs) treatment satisfactorily, 23.1% of patients required additional low-dose corticosteroids, and only 7.6% of patients received further immunosuppressive	(88)

					PET/CT. Five patients had inflammation in their joints damaged before osteoarthritis. In 11 patients, joint pain could not be determined.	therapy. The treatment effect of arthralgia patients is better, and PFS and OS are improved.	
Noguchi (2018)	Granulomatous lesions	/	Nodular granulomatous reaction	Nivolumab	An 81-year-old male with cT1aN2M1b stage IV pleomorphic cancer of the left upper lobe was treated with nivolumab as a secondary treatment. The swelling of the left supraclavicular lymph node and left adrenal gland was reduced, but the shadow of the tumor in the right upper lobe increased. A bronchoscopy was done, and the biopsy showed a granuloma; the result was similar to a sarcomatoid granuloma reaction.	With the withdrawal of nivolumab, the shadow finally disappeared;	(90)

Al-Dliw (2017)		Melanoma	Pembrolizumab	Distant granulomatous infection	The patient was a 65-year-old white woman with stage III, T3B, and N2A superficial melanoma of the left hip. Pembrolizumab was used for one year. The biopsy results showed chronic granulomatous inflammation of histiocytes and no malignant tumors were found.	The patient started receiving high-dose intravenous steroids and showed significant clinical improvement.	(89)
Nikolakis (2019)	Others	Malignant melanoma	Swollen mediastinal lymph nodes	Pembrolizumab	A patient with malignant melanoma was treated with pembrolizumab for three months. Although the skin metastases had a partial response, the patient still developed enlarged mediastinal lymph nodes	Perform selective lymph node removal. The histopathological results are consistent with nodular reactions. Treatment was interrupted, and systemic steroid pulse therapy resulted in significant relief of lymphadenopathy	(91)

Lederhandle r (2018)		Lung adenocarci noma	Grade 3 ulcerative oral mucositis	Pembrolizum ab	A 78-year-old woman developed grade 3 ulcerative oral mucositis 13 months after starting the PD-1 inhibitor pembrolizumab for lung adenocarcinoma	She was successfully treated with prednisone and the oncologist temporarily used pembrolizumab	(92)
Yatim, N. (2018)		/	Lung and skin sarcoidosis	Pembrolizu- mab	/	Treating sarcoidosis as a potential side effect of pembrolizumab treatment is the key to avoiding misdiagnosis of malignant lesions	(128)
Zheng (2020)			Off-target effects caused by BTK gene mutations	Anti-PD- 1/PD-L1 drugs	/	/	(129)
Parakh, S.		Metastatic	Delayed	Nivolumab	Patients with metastatic melanoma	Even after treatment is	(93)

(2018)		melanoma.	autoimmune disease		have delayed autoimmunity after stopping treatment with the anti-pd-1 antibody nivolumab for 8 months	stopped, patients receiving immune checkpoint inhibitor therapy need to be continuously monitored, especially as patients increasingly stop treatment after obtaining a durable response.	
Gauci, M.L. (2017)		Melanoma	RS3PE syndrome	Nivolumab	Inflammatory arthralgia, synovitis of proximal interphalangeal joint, wrist joint and ankle joint, edema of hands and forearm occurred in the 4th week after receiving niluzumab treatment. RS3PE syndrome	Systemic corticosteroid therapy was started (0.5mg/kg/d); nilumab was maintained for 4 weeks, the clinical symptoms were relieved within 10 days, the C-reactive protein level was normalized, and there was no recurrence when nilumab recovered. Corticosteroids	(130)

						gradually decreased and stopped using it after 9 months. After 5 months, due to disease progression, anti-PD1 stopped completely.	
Uemura, M. (2017)		/	Grover's disease	Ipilimumab	Ipilimumab induces Grover's disease	Th2 cells may be pathogenic mediators	(131)

PD-1, programmed cell death protein 1; PD-L1, programmed cell death protein ligand 1; irAEs, immune-related adverse events; RS3PE, remitting seronegative symmetrical synovitis with pitting edema. For reference citation please see the reference list in the main manuscript.