



Appendix 2

Table 4. Case reports and case series of steroid-refractory ICI myocarditis treated with infliximab

Author and date	Patient details	1 st -line treatment	Additional immunosuppressant treatment	Outcomes	Cited in reviews
Case reports					
Vu et al. 2025 ¹⁹ (conference abstract)	A 74-year-old man with right renal clear cell carcinoma who presented for shortness of breath and bradycardia, four weeks after completing one cycle of neoadjuvant pembrolizumab and lenvatinib.	methylprednisone 1000 mg for 3 days then 1 mg/kg	One dose of iv infliximab, 5 mg/kg was given.	Heart rhythm recovered to atrial fibrillation; ejection improved to 55%; patient extubated.	-
Gomez et al. 2025 ²⁰	An 80-year-old man receiving pembrolizumab as first-line treatment for MSI locally advanced gastric adenocarcinoma, presented 3 weeks after the second dose of ICI with progressive fatigue, muscle weakness, blurred vision, binocular diplopia and left ptosis. ICI-induced myocarditis, myositis and myasthenia gravis overlap (triple M) syndrome was established	intravenous methylprednisolone 1.5 mg/m ² – no clinical improvements after 3 days	iv methylprednisolone (1 g/day), iv immunoglobulin (IVIG) 2 mg/kg over 5 days and iv infliximab 500 mg	Gradual improvement of CV symptoms	
Tan et al. 2024 ¹⁶	A 62-year-old man presented with dizziness, bilateral ptosis	Methylprednisolone 80 mg/day then	IVIG (20 g/ day) and MMF (1,000 mg/day) for	Symptoms resolved gradually	Tan 2024 ¹⁶

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	<p>and eye movement disorders 2 weeks after 2 cycles of ICI combination treatment. The diagnosis of ICI-induced myocarditis (grade 3), and myositis-myasthenia gravis overlap syndrome was diagnosed.</p> <p>A 57-year-old woman with lung cancer diagnosed with grade 3 ICI-induced myocarditis after 3 cycles of ICI treatment. Symptoms initially improved with steroid treatment by on day 16 and steroid-refractory ICI-induced myocarditis was diagnosed.</p>	<p>pulse dose methylprednisolone 500 mg/day for 7 days.</p> <p>Methylprednisolone (80 mg/day for 9 days, with gradually decreasing doses)</p>	<p>6 days. Symptoms persisted; elevated TNF-alpha detected. Infliximab (200 mg/day) was given on Days 23, 37 and 64.</p> <p>Pulse-dose methylprednisolone (500 mg/day) for 3 days, MMF (1,000 mg/day) for 11 days and IVIG (20 g/day) for 3 days. Elevated TNF-alpha detected. Infliximab (200 mg) was administered on Days 31, 45 and 73. Oral prednisone (50 mg/day, tapering dose).</p>	Symptoms resolved	
Feng et al. 2024 ²⁵	A 58-year-old man with thymoma was diagnosed with myocarditis after treatment with toripalimab. Also diagnosed with myasthenia with positive anti-acetylcholine receptor antibodies.	Corticosteroids (250 mg/q12h) and immunoglobulin (400 mg/kg for 5 days) administered, with little improvement.	Two weekly infusions of infliximab	Myocarditis improved	Tan 2024 ¹⁶

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Koelmeyer et al. 2024 ⁴²	A 68-year-old woman with urothelial cancer who developed shortness of breath and chest pain one week after receiving combination ICI therapy. Her condition deteriorated, with reduced ejection fraction.	Pulse-dose methylprednisolone	Additional anti-inflammatory agents administered, including mycophenolate, infliximab, and anti-thymocyte globulin.	Little improvement in clinical status; the patient died.	
Qin et al 2024 ²¹	A retrospective review of 31 patients with ICI-induced myocarditis; 21 had grade 3-4 myocarditis. One 36-year-old man developed grade 4 myocarditis after 1 treatment cycle.	Methylprednisolone 500 mg	The patient was given IVIG, infliximab (300 mg) and plasmapheresis	Symptoms improved; no myocarditis relapse. Patient died of cancer progression	
Eslinger et al. 2023 ²⁹	An 85-year-old man presented with significant chest pain and progressive shortness of breath after a second infusion of pembrolizumab. A diagnosis of grade 4 myocarditis was made and the ICI treatment was stopped. He was discharged after initial treatment, but presented with symptoms on myocarditis on 3 separate occasions; refractory myocarditis was considered.	Methylprednisolone at 1,000 mg for 3 days followed by 60 mg of oral prednisone daily, tapered by 10 mg every 7 days.	One dose of 5 mg/kg infliximab with pulsed methylprednisolone at 1,000 mg for 3 days and transitioned to a slow prednisone taper.	Symptoms resolved; no recurrence of myocarditis.	Wang 2024 ¹⁵
Deharo et al. 2022 ²⁷	A 70-year-old man was admitted to intensive care after 2 cycles of ICI therapy; diagnosed as grade 3/severe	Methylprednisolone 1000 mg/day	Infliximab 500 mg Patient then developed atrio-ventricular block treated with a	Patient died.	Wang 2024 ¹⁵

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	ICI-induced myocarditis, myositis and myasthenia gravis syndrome.		pacemaker; Abatacept (500 mg) and five sessions of plasmapheresis.		
Kadokawa et al. 2021 ³⁰	A 66-year-old man developed disseminated intravascular coagulation (DIC) and myocarditis after ICI therapy.	Prednisolone 80 mg iv days 34–36; methyl prednisolone sodium succinate 1000 mg iv days 37–39; prednisolone 80mg iv days 40-44	Day 40: infliximab (5 mg/kg); prednisolone dose tapered; Day 54 second dose of infliximab (5 mg/kg)	Day 49 – DIC improved; Day 69 – myocarditis improved	Tan 2024 ¹⁶ CADTH 2024 ³ Wang 2024 ¹⁵
Barry et al. 2021 ²³	An 82-year-old man with urothelial cancer developed ICI myocarditis	Methylprednisone 1g daily for 5 days	IVIg then single dose of infliximab (due to concomitant myositis)	No improvement; ATG started and symptoms improved.	Wang 2024 ¹⁵
Portoles-Hernandez et al. 2021 ²⁶	A 48-year-old woman with thymoma who developed complete atrioventricular block associated with fulminant myocarditis and myasthenia gravis 2 weeks after starting pembrolizumab.	Methylprednisolone dose (2 mg/kg)	Infliximab (5 mg/kg) was administered, a temporary pacemaker implanted and methylprednisolone dosage escalated (1 g per day, intravenously, for 5 days), and subsequently continued with previous dose (2 mg/kg)	Developed cardiogenic shock and respiratory failure; died 10 days after admission.	Phing 2024 ¹⁴ Cozma 2022 ¹⁷
Puzanov et al. 2021 ⁴³	A retrospective study of 15 patients who had ICI-associated myocarditis; 11 of whom had severe (grade 3–4) myocarditis. One patient had	Patient given infliximab started on oral prednisone 160 mg twice daily, and had two doses of iv	Patient given infliximab on Day 86, then oral prednisone.	Myocarditis resolved.	Tan 2024 ¹⁶

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	additional treatment with infliximab.	methylprednisolone 1 g at Day 29 and Day 81.			
Wang et al. 2021 ³⁹	Case series of 24 patients with ICI-induced myocarditis. One patient with corticosteroid-resistant myocarditis given infliximab.	Corticosteroids Methylprednisolone iv 500 mg	Single dose of infliximab (500 mg iv)	No improvement – death from myocarditis progression	Daetwyler 2024 ⁵
Wintersperger et al. 2021 ⁴⁰	A series of 4 patients with ICI-induced myocarditis. One patient's myocarditis improved after high-dose steroids but he was readmitted 79 days after initial presentation and given infliximab and mycophenolate.	Methylprednisolone 1 g for 5 days then oral prednisone 2 mg/kg	Infliximab 350 mg and mycophenolate mofetil iv (1000 mg twice daily)	Symptoms improved.	Cozma 2022 ¹⁷
Dearden et al. 2021 ²²	Of 82 patients who developed hyperacute toxicity after treatment with ipilimumab and nivolumab, two developed myocarditis (grade 5, with death 16 days and 24 days after treatment).	Not specified	One patient received 2 days of infliximab.	Patients died from myocarditis.	
Giancaterino et al. 2020 ³¹	An 88-year-old man who developed generalised weakness 22 days after a first dose of nivolumab for melanoma. Steroids were started for suspected myocarditis, but he developed heart block.	Methylprednisolone 125 mg daily iv on Days 5–6; then increased to 1 g iv methylprednisolone daily	One dose of infliximab 5 mg/kg given on Day 9.	Symptoms did not improve; pacemaker fitted; patient died on Day 15.	Tan 2024 ¹⁶ Phing 2024 ¹⁴ Cozma 2022 ¹⁷ Wang 2024 ¹⁵

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Fuentes-Antras et al. 2020 ²⁸	A 75-year-old man with lung adenocarcinoma who presented with hyperthyroidism and mild hepatotoxicity after a single cycle of ICI therapy that led to thyrotoxicosis and hepatitis.	High-dose dexamethasone (4 mg every 6 h) 1 g iv methylprednisolone bolus daily for 5 days	Infliximab 5 mg/kg then iv immunoglobulins	Infliximab and IVIG started due to rapid progression to myocarditis, pneumonitis and MG. Death on Day 7.	Phing 2024 ¹⁴ Cozma 2022 ¹⁷
Norwood et al. 2020 ⁴⁴	A 57-year-old woman developed ICI-induced myocarditis treated with steroids. After 15 months another dose of ICI therapy was given and myocarditis recurred.	Methylprednisolone 125 mg/day for 12 days, followed by prednisone 1 mg/kg/day	A single dose of infliximab	No improvement after infliximab – treated with ATG, tacrolimus, mycophenolate and prednisone and symptoms improved,	Cozma 2022 ¹⁷
Pdegimas et al. 2019 ³²	53-year-old woman with metastatic ovarian adenocarcinoma who had increased troponin 4 days after starting pembrolizumab treatment. She was discharged on 50 mg of prednisone but presented one month later with exertional chest pressure and myocarditis was diagnosed.	Prednisone 1 mg/kg was started, then 1 g methylprednisolone for 3 days.	Symptoms recurred after steroid taper and infliximab (5 mg/kg) was given.	Arrhythmias terminated and she was discharged on steroid taper. Troponin normalised in 9 months.	Tan 2024 ¹⁶ Phing 2024 ¹⁴ CADTH 2024 ³
	A 62-year-old woman with metastatic renal cell carcinoma who developed sudden dyspnoea 5 weeks after starting nivolumab	Methylprednisolone iv 1 mg/kg; then 2 g methylprednisolone for 3 days.	One dose of infliximab (5 mg/kg) given after 3 days.	Conduction block resolved; she had a single-chamber cardioverter-defibrillator placement and	

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	treatment. She developed cardiogenic shock and finding were consistent with perimyocarditis.			recovered from cardiogenic shock. She died 2 months later of bacteraemia and pulmonary embolism.	
Saibil et al. 2019 ³³	A 67-year-old man with metastatic melanoma treated with ipilimumab and nivolumab developed increasing fatigue, weakness and dyspnoea 16 days later. Myocarditis was diagnosed.	High-dose methylprednisone (200 mg on Day 1, then 1000 mg daily for 3 days)	Symptoms worsened – given one dose of infliximab (5 mg/kg) and 2 doses of intravenous immunoglobulin.	Condition worsened and he died on Day 18 of multiple organ failure including myocarditis and rhabdomyositis.	Tan 2024 ¹⁶ Daetwyler 2024 ⁵ CADTH 2024 ³ Phing 2024 ¹⁴ Cozma 2022 ¹⁷ Wang 2024 ¹⁵
Gallegos et al. 2019 ⁴¹	A 47-year-old woman with a history of carotid artery dissection and metastatic melanoma presented with acute heart failure, 4 months after restarting nivolumab. LVEF = 26%	Methylprednisolone 500 mg intravenous BID for 5 days	Infliximab (10 mg/kg/day for 2 days)	Symptoms worsened and patient died	Tan 2024 ¹⁶ Phing 2024 ¹⁴
Shah et al. 2019 ⁴⁵	A 73-year-old man with urothelial carcinoma who developed ICI-induced myocarditis.	Methylprednisolone iv (1 mg/kg twice daily), with mild response	A single infliximab infusion followed by 12 rounds of plasmapheresis, and subsequent IVIG infusions.	Underwent a tracheostomy; death primarily due to cancer progression.	Phing 2024 ¹⁴
Agrawal et al. 2019 ³⁴	A case series of 5 patients with ICI-related cardiotoxicity, including one patient, a 67-year-old man with melanoma treated with nivolumab, who received infliximab for recurrent myocarditis.	Pulse dose steroid (1,000 mg/day) given for 3 days then prednisolone (80 mg BID)	Infliximab 5 mg/kg for two doses.	Myocarditis improved after second infusion; no cardiovascular mortality in 120 days of follow-up	Tan 2024 ¹⁶ Phing 2024 ¹⁴

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Zlotoff et al. 2019 ³⁵ Conference abstract	An 88-year-old man developed fatigue after starting pembrolizumab for metastatic melanoma. He was diagnosed with ICI myocarditis after endomyocardial biopsy and increased troponin levels.	Methylprednisolone 1 g iv daily	After 5 days, troponin increased to 719 ng/L and 5 mg/kg infliximab was given. Troponin continued to rise and a second dose of infliximab was given and mycophenolate mofetil started: 750 mg twice daily. Troponin increased further.	Discharged after 3 weeks; continued oral prednisone 60 mg daily and mycophenolate mofetil 1000 mg twice daily and had two infusions of intravenous immunoglobulin. His troponin values gradually fell to 578 ng/L at one month after discharge.	Phing 2024 ¹⁴
Frigeri et al. 2018 ³⁶	A 76-year-old woman with lung adenocarcinoma in remission after 7 bi-weekly treatments with nivolumab, who developed signs of heart failure and developed cardiogenic shock. LVEF <10%	Methylprednisolone (5 mg/kg/day) then plasmapheresis and IVIG (1000 mg/kg/day)	Infliximab 5 mg/kg on Day 6, Day 27 and Day 39 (3 doses)	Myocarditis improved; no cardiovascular mortality in 180 days of follow-up	Tan 2024 ¹⁶ Phing 2024 ¹⁴ Cozma 2022 ¹⁷
Martinez-Calle et al. 2018 ³⁷	A 67-year-old woman with multiple myeloma who developed myocarditis after starting pembrolizumab treatment.	Methylprednisolone 1.5 mg/kg/day	Infliximab 5 mg/kg – one dose	No improvement; patient died of multi-organ failure	Tan 2024 ¹⁶ Phing 2024 ¹⁴ Cozma 2022 ¹⁷
Tay et al. 2017 ³⁸	A 64-year-old woman with glioblastoma developed arrhythmias secondary to histologically confirmed severe immune-mediated myocarditis. LVEF = 37%	Methylprednisolone 500 mg daily for 3 days before tapering to oral prednisolone 100 mg daily.	A single dose of iv infliximab 5 mg/kg administered on Day 2	Myocarditis did not improve after infliximab; symptoms improved after ATG then mycophenolate	Tan 2024 ¹⁶ Daetwyler 2024 ⁵ Phing 2024 ¹⁴ Cozma 2022 ¹⁷ Wang 2024 ¹⁵

Author and date	Patient details	1 st -line treatment	Additional immunosuppressant treatment	Outcomes	Cited in reviews
Johnson et al. 2016 ²⁴	A 63-year-old man with metastatic melanoma developed fatigue and myalgias 15 days after a first dose of ICI therapy. Myocarditis and myositis were diagnosed. LVEF = 50%	Methylprednisolone iv administered at 1 g/kg daily for 4 days	Infliximab 5 mg/kg – one dose	Complete heart block developed followed by cardiac arrest and death.	Tan 2024 ¹⁶ Phing 2024 ¹⁴
Retrospective cohort studies, case series					
Ali et al. 2024 ⁴⁹	A single-centre, retrospective cohort study of 99 patients with ICI-induced myocarditis. 44 of 65 (68%) of patients with cytokine data available had peak TN-alpha above normal limits (>22 pg/mL). 50 patients had grade 3 or 4 myocarditis.	81 patients given steroids and 61 given immunomodulators	23 patients given infliximab (5 mg/kg): included 6 with TNFalpha ≥22 pg/ml and 16 with TNF-alpha >22 pg/ml. Administration of infliximab showed similar MACE-free and overall survival between all patients and those with elevated TNF-alpha levels.	None of the patients who received infliximab developed worsening heart failure after infliximab administration. Conclusion: the use of infliximab did not lead to different survival outcomes.	
Zhang et al. 2021 ⁴⁶	A retrospective case series of 11 patients who developed ICI-induced myocarditis; 4 patients (mean age 61.8 years) had grade 4 myocarditis treated with infliximab due to worsening clinical status despite high-dose steroids (refractory myocarditis).	High-dose steroids - iv methylprednisolone 1 g x 3 days	All 4 patients received a single dose of infliximab (5 mg/kg).	All 4 patients survived initial hospitalisation but needed prolonged steroid tapers. Two patients died from septic shock 2 and 3 months after initial myocarditis treatment. The other 2 patients completed steroid tapers with no evidence of myocarditis.	Tan 2024 ¹⁶ Daetwyler 2024 ⁵ CADTH 2024 ³

Author and date	Patient details	1 st -line treatment	Additional immunosuppressant treatment	Outcomes	Cited in reviews
Lipe et al. 2021 ⁴⁷	Retrospective chart review of 7 patients with ICI-associated myasthenia gravis, myositis and myocarditis overlap syndrome. 4 patients had confirmed myocarditis by an endomyocardial biopsy.	High-dose glucocorticoids (1–2 mg/kg of prednisone or equivalent)	Three patients with confirmed myocarditis given infliximab.	All three patients needed further treatments after infliximab; these were rituximab and plasma exchange in 2 patients who survived; the 3 rd patient had plasma exchange and IVIG but died.	Tan 2024 ¹⁶
Cautela et al. 2020 ⁴⁸	A case-control study of 60 patients (aged 69 ± 12 years) who developed ICI-induced myocarditis. 36 patients had grade 4 myocarditis and required IIST; 20 patients had grade 3–4 myocarditis and did not require IIST.	High-dose corticosteroids	36 patients required IIST: 8 were treated with infliximab. Patients who received infliximab were more likely to die from cardiovascular causes (OR, 12.0; 95% CI 2.1 to 67.1; p=0.005).	5 patients died, 4 of cardiovascular causes. In patients receiving IIST, infliximab treatment was associated with a significantly increased risk of cardiovascular death.	

ATG: anti-thymocyte globulin; CI: confidence interval; ICI: immune checkpoint inhibitor; IIST: intensified immunosuppressive therapy; IVIG: intravenous immunoglobulin; IV: intravenous; MACE: major adverse cardiovascular events; MG: myasthenia gravis; MMF: mycophenolate mofetil; OR: Odds ratio