Supplementary

Table S1 Timeline of events from diagnosis of malignant mesothelioma to last follow-up

Timeline	Patient diagnosed with malignant mesothelioma
2 years prior to presentation	• Initial admission to hospital due to unknown weight loss (12 kg in <6 months) and abdominal pain • PET-CT scan: supradiaphragmal, pleural tumor with diaphragmatic infiltration and suspicious peritoneal lymph node involvement (cT4cN1 MX) • Cytoreductive surgery with HIPEC: partial diaphragmatic resection with alloplastic reconstruction, subtotal parietal peritonectomy, with partial resection of the ribs 9–12, followed by HIPEC • Histopathologic examination: malignant epithelioid mesothelioma: pT2 pN1 (2/5 LK) M0 (UICC stage II) • KPS 90%
1 year prior to presentation	Recurrent disease with new pleural and perihepatic metastases, as assessed by PET-CT
9 months prior to presentation	Next-generation sequencing was performed showing no targetable mutations using Oncomine Precision Assay (Thermo Fisher Scientific, 168 Third Avenue Waltham, MA USA 02451).
7 months prior to presentation	Patient undergoes stereotactic body radiotherapy (5×8 Gy) to the basal and lateral pleural metastases and interstitial brachytherapy (1×20 Gy) to liver metastasis
3 months prior to presentation	Progressive disease with multiple new bipulmonary and lymph node metastases with diffuse, extensive spread throughout the abdomen (PET-CT) • Tumor board decides on the initiation of immunotherapy with anti-PD-L1 agent pembrolizumab
1 month prior to presentation	Pembrolizumab (1st cycle)
1 week prior to presentation	Pembrolizumab (2nd cycle); onset of irAEs and hospital admission
Upon emergent presentation	Patient presents with generalized weakness, shortness of breath, double vision and ptosis • Physical findings significant for MG • Severely reduced EF (<35%); ST segment elevation in the posterior leads with polymorphic ventricular extrasystoles • Elevated cardiac biomarkers • Clinical criteria suggestive of ICI-associated myocarditis
Day 1 to Day 10 following emergent presentation	Patient on i.v. methylprednisolone (100 mg/die) Coronary artery disease ruled out by negative cardiac catheterization Respiratory failure due to MG, patient is intubated Upon clinical improvement, patient is extubated, NIV is continued due to hypercapnia
Day 11 to Day 30 following emergent presentation	Patient develops arrhythmias with hemodynamic compromise (atrial fibrillation and flutter, ventricular tachyarrhythmias) • Electrical and pharmacological cardioversion • Reintubation and reventilation • No remarkable improvement despite steroids • Initiation of plasma exchange, clinical improvement and stabilization, steroid tampering, extubation • EF recovery (45–50%)
Day 30 following emergent presentation	Discharge to external weaning ward, oral prednisone, KPS 50%

Table S1 (*continued*)

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Table S1 (*continued*)

Timeline	Patient diagnosed with malignant mesothelioma
6 months after administration of pembrolizumab	Discharge from weaning ward and rehabilitation clinic to home; CT scan of thorax showing stable disease according to RECIST, version 1.1
1 year following administration of pembrolizumab	Patient presents with dysphagia, KPS 70% • Progressive disease (CT) with new pulmonary metastases and extrinsic compression of the oesophagus • EF appr. 50%, sinus tachycardia with extrasystoles • Initiation of palliative therapy (oesophagus stenting) • Patient exhibits hypercapnia and respiratory failure, continues to deteriorate with Existus letalis due to respiratory failure

PET-CT, positron emission tomography-computed tomography; HIPEC, heated intraperitoneal chemotherapy; KPS, Karnofsky performance status; PD-L1, programmed death-ligand 1; irAEs, immune-related adverse events; MG, myasthenia gravis; EF, left-ventricular ejection fraction as assessed by transthoracic echocardiography; ICI, immune-check-point inhibitors; NIV, non-invasive ventilation; RECIST, response evaluation criteria in solid tumors.

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Table S2 Selected case reports on ICI-associated myocarditis with use of therapeutic plasma exchange

Case report	Causative agent	Oncological indication	irAEs	Steroid regimen	Plasma exchange	Other therapies	Outcome
Kimura *et al.* (2016)	Nivolumab	Malignant melanoma	Myocarditis, myositis and myasthenic crisis	3 days of steroid pulse therapy (1,000 mg/day) followed by oral prednisolone at a dose of 1 mg/kg, which was tapered to 20 mg/day	7 cycles	IVIG (400 mg/kg/day), immune absorption	Survived 4 months of intensive care; rehabilitation with maintenance therapy of 20 mg/day prednisolone and low-dose pyridostigmine
Arangalage *et al.* (2017)	Ipilimumab/ nivolumab	Malignant melanoma	Myocarditis	1,000 mg Methylprednisolone daily	3 cycles	IVIG, Tacrolimus, ECMO	Clinical improvement, alive at 3-month follow-up
Frigeri *et al.* (2018)	Nivolumab	Adenocarcinoma of the lung	Myocarditis	Methylprednisolone 5 mg/kg/day	1 cycle	IVIG (1 g/kg), Infliximab (2×5 mg/kg)	Alive, discharged at home
Nasr *et al.* (2018)	Pembrolizumab	Gastric adenocarcinoma	Myositis, myocarditis and ophthalmoplegia	Prednisone 1–2 mg/kg, followed by pulse steroid therapy	Yes, but not contributory to clinical improvement. Detailed information not available.	IVIG, Methotrexate	Clinical worsening, exists within days
Shirai *et al.* (2018)	Pembrolizumab	Malignant melanoma	MG, myositis, myocarditis	3 day of steroid pulse therapy (Methylprednisolone 1,000 mg/d), followed by prednisolone at a dose of 1 mg/kg/d, then tapered to 30 mg/d	4 cycles		Clinical improvement, alive at 6-week follow-up
Fazel, Jedlowskil (2019)	Nivolumab/ ipilimumab	Malignant melanoma	MG, myositis, myocarditis, transaminitis	Methylprednisolone 1.5–2 mg/kg, pulse therapy with 1,000 mg/day	1 cycle	IVIG 2 mg/kg for 2 days	Clinical worsening, initiation of palliative care and discharge to inpatient hospice care

Table S2 (*continued*)

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Table S2 (*continued*)

Case report	Causative agent	Oncological indication	irAEs	Steroid regimen	Plasma exchange	Other therapies	Outcome
Shah *et al.* (2019)	Nivolumab/ ipilimumab (two patients) and atezolizumab, respectively (one patient)	Urothelial carcinoma (two patients) and melanoma (one patient), respectively	MG, myasthenic syndrome, myocarditis	Methylprednisolone 1–2 mg/kg	5–12 cycles	Infliximab, pyridostigmin	Mixed. Clinical improvement, exists due to cancer progress (two patients); clinical improvement and alive at 12-month follow-up (one patient)
Esfahani, Buhlaiga (2019)	Pembrolizumab	Malignant melanoma	MG-myositis overlap syndrome, myocarditis	Pulse Methylprednisolone 1 g per day for 3 days	5 cycles	Mycophenolate mofetil, rituximab, alemtuzumab	Clinical improvement, alive at 4-month follow-up
Jeyakumar (2020)	Cemiplimab	Cutaneous squamous cell carcinoma	MG, myositis, myocarditis	High-dose Methylprednisolone	5 cycles	IVIG for 1 day	Exists due to cardiac arrest
Xing *et al.* (2020)	Sintilimab	Adenocarcinoma of the lung	MG-myositis overlap syndrome, myocarditis	Methylprednisolone 2 mg/kg/day	2 cycles	IVIG (400 mg/ kg/d for 5 days)	Survived 3 months of intensive care; rehabilitation and maintenance therapy pyridostigmine bromide without prednisone, as well as mechanical ventilation (12 hours per day)

ICI, immune-check-point inhibitors; irAEs, immune-related adverse events; IVIG, intravenous immunoglobulin; ECMO, extracorporeal membrane oxygenation; MG, myasthenia gravis.

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