

**Table S1.** Overview of published case-reports regarding central nervous system manifestations as neurological adverse events of ICI-therapy. Besides patients' clinical data certain diagnostic findings as well as immunosuppressive.

author	year	patient age	patient sex	underlying disease	ICI therapy	neurological symptoms	latency ICI-start/onset irAE	CSF findings	brain MRI	antibody findings	immunosppr. therapy	outcome	others
Bossart et al [1]	2017	60	female	metastatic melanoma, cerebral metastases	ipilimumab + pembrolizumab	<b>encephalitis</b> (generalized weakness, tiredness)	12 weeks	n.d.	inconspicuous	n.d.	n.d.	death	autopsy: infiltrates of CD8+ lymphocytes esp. In brainstem
Burke et al [2]	2018	64	female	clera-cell ovarian cancer	nivolumab	<b>encephalitis</b> (fever, spasms, delirium)	17 weeks	n.d.	inconspicuous	GAD-antibody positive	methylpredn. i.v., plasmapheresis	major improvement	
Maurice et al [3]	2015	60	male	metastatic melanoma	ipilimumab + nivolumab	<b>encephalitis</b> (subacute confusion, nausea, vomiting, psychomotor slowing)	8 weeks	cc 0, protein 0.88 g/l, myelin-basic protein positive	tumefactive demyelination	n.d.	methylpredn. i.v., IVIG	improvement	CD4+ and CD8+ T-cell infiltration of spinal cord
Richard et al [4]	2017	74	male	NSCLC	nivolumab	<b>encephalitis</b> (dysarthria, weakness of lower limbs)	1 week	inconspicuous	n.d.	negative	methylpredn. i.v.	improvement	
Schneider et al [5]	2017	78	male	squamous cell carcinoma lung	nivolumab	<b>encephalitis</b> (apathy, aphasia, myoclonuses)	28 weeks	cc 16, lactate 4.1 mol/l, protein 1.03 g/l	inconspicuous	negative	methylpredn. i.v.	major improvement	
Williams et al [6]	2016	55	female	metastatic melanoma, cerebral metastases	nivolumab + ipilimumab	<b>encephalitis</b> (memory loss, gait disturbance, fever, inappropriate laughing)	1 week	cc 8, glucose and protein normal	inconspicuous	NMDA-R-antibodies positive in CSF	methylpredn. i.v., IVIG	no improvement, after rituximab	
		65	male	SCLC	nivolumab + ipilimumab	<b>encephalitis</b> (short-term memory loss,	4 days	cc 18, protein 0.98 g/l	nonspecific T2 hyperintense	antigliab nuclear antibody	prednisone 60 mg/d	dramatic improvement	

					b	progressive gait disturbance)			se lesion right mesial ltemporal lobe	(SOX-1), serum			
<b>Kawamura et al [7]</b>	2016	54	female	adeno-carcinoma lung, cerebral metastases	nivolumab	<b>cerebellitis</b> (dizziness, nausea, nystagmus, cerebellar ataxia)	2 weeks	cc 10, protein 0.56 g/l	inconspicuous	negative	methylpredn. 1g/d, 3 days	major improvement	patient died due to pneumonia
<b>Narumi et al [8]</b>	2018	75	male	squamous cell carcinoma lung	nivolumab	<b>NMOSD</b> (acute bilateral paralysis, sensory loss below Th10)	8 weeks	cc 1195, protein 3.8 g/l	brain MRI: inconspicuous; <b>spinal:</b> T2 hyperintense lesions C5-6, Th12-L1	AQP4, serum	methylpredn. i.v., plasmapheresis	minimal improvement	
<b>O'Kane et al [9]</b>	2014	58	male	metastatic melanoma	ipilimumab	<b>Myelitis</b> (weakness left leg, sensory deficit below Th10, constipation, micturition disturbance)	24 weeks	cc 16, protein 0.57 g/l	brain MRI: inconspicuous; <b>spinal:</b> T2 hyperintense lesion Th7-L1	negative	methylpredn. i.v., IVIG 5 days	little improvement	colitis, day 16 after therapy start
<b>Tan et al [10]</b>	2018	65	male	metastatic melanoma	nivolumab + ipilimumab	<b>neurosarcoidosis</b> (transient aphasia, visual field defects, mental status deficits)	52 weeks	cc 13, protein 0.75 g/l	leptomeningeal enhancement left occipital and parietal lobes	n.d.	methylpredn. i.v., dexamethasone 16 mg/d; infliximab 5mg/kg; MTX 12,5 mg/week	improvement	
<b>Salam et al [11]</b>	2016	64	male	metastatic melanoma	pembrolizumab	<b>limbic encephalitis</b> (progressive decline in memory MMSE 22/30)	52 weeks	cc 17, protein 0.53 g/l	bilateral symmetric T2 hyperintense, hippocampi, anterior temporal lobe, insula atrophy	negative	methylpredn. i.v.	no improvement, no decline	
<b>Stein et al [12]</b>	2015	56	male	metastatic melanoma	ipilimumab	<b>meningoencephalitis</b> (diaphoresis,	15 weeks	cc 705 (96%	initially negative;		methylpredn. i.v.	complete recovery	

						fevers, declining mental status)		lymphos) protein 2.2 g/l	Repeat: abnormal diffuse dural thickening with enhanceme nt		160 mg/d	
<b>Khoja et al [13]</b>	2016	51	female	metastatic melanoma	pembrolizumab	<b>acute encephalopathy</b> and eosinophilic fasciitis (headache, visual field floaters, movement difficulty; thickened waxy skin; confusion)	76 weeks	cc normal, protein 0.27 g/l	hyperintense white matter foci subcortical and periventricular, all with restricted diffusion new enhancing lesion centrum semiovale left; follow-up: two new lesions FLAIR	n.d.	methylpredn. i.v.	slight improvement
<b>Gettings et al [14]</b>	2015	56	male	metastatic melanoma	ipilimumab	<b>MS relapse</b> (new gait dysfunction, ataxia)	4 weeks	n.d.	hyperintensity parasagittal, frontoparietal, temporal-occipital FLAIR	n.d.	methylpredn. i.v. 500 mg 3 days; glatiramer acetate + steroids	
<b>LaPorte et al [15]</b>	2017	26	female	Hodgkin's Lymphoma	ipilimumab, pembrolizumab	<b>PRES</b> (grand mal seizure)	1.5 weeks	n.d.	hyperintense lesions posterior white-matter region: cerebellar,	n.d.	none	improvement
<b>Maur et al [16]</b>	2012	58	female	metastatic melanoma	ipilimumab	<b>PRES</b> (acute blindness, headache, generalized seizures)	2 weeks	n.d.		n.d.	cortisone acetate (s. adrenohypophysitis)	complete recovery

<b>Mandel et al [17]</b>	2014	66	male	metastatic melanoma	ipilimumab, lambrolizumab	ataxia, vertigo, numbness left arm; convulsive status	10-12 weeks	cc 6, protein 1.03 g/l	parieto-occipital 1. brain MRI: unremarkable (motion artifact); 2. brain MRI: FLAIR hyperintensities bilat. Claustrum + right frontal and left occipital lobes	n.d.	none (anticonvulsive therapy)	complete recovery	open biops, lymphocytic infiltrates of right frontal lesion: diffuse microglial activation
<b>Bompaire et al [18]</b>	2012	56	male	metastatic melanoma	ipilimumab	<b>meningo-radiculoneuritis</b> (vertigo, dizziness, headache; rep. falls, dysarthria, dysaesthesia; severe gait ataxia, tetraplegia)	10 weeks	1. cc 135, protein 5 g/l; 2. cc 104, protein 4.45 g/l	brain MRI: inconspicuous; <b>spinal MRI</b> : global enhancement of nerve-roots	negative	oral prednisone 80 mg/d; methylpredn. i.v. 1g/d 3 days, IVIG 0,4g/kg/d 5 days + oral prednisone 1 mg/kg/d 4 months	almost complete recovery after 24 months	two conduction blocs (left perone, right cubital), acute deervation lower limbs
<b>Altman et al [19]</b>	2015	32	male	metastatic melanoma	ipilimumab	<b>bilateral facial palsy</b>  hypophysitis 11/2011; <b>encephalopathy</b> 08/2012 +	5 weeks	n.d.	n.d.	n.d.	oral prednisone 80- 100 mg/d	improvement	
<b>Carl et al [20]</b>	2015	64	male	prostate cancer	ipilimumab	autoimmune thyroiditis: SREAT (adynamia, memory disturbances; myocloni,	52 weeks	cc normal, protein 0,85 g/l	mild microangiopathic changes	negative	oral prednisolone 50 mg/d; methylpredn. i.v. 1g/d 3 days	major improvement	

<b>Conry et al [21]</b>	2015	41	male	metastatic melanoma	ipilimumab	seizures) <b>encephalopathy</b> (fever, headache, myalgia; expressive aphasia, gait ataxia), peripheral symptoms (sensory neuropathy, neurogenic bladder)	7.5 weeks	cc 128, minimally elevated protein	cMRI: restricted diffusion/FLAIR hyperintensity posterior splenium of corpus callosum	negative	oral prednisone 30 mg/d; later 1 mg/kg; methylpredn. i.v. 2mg/kg 5 days	major improvement
<b>Wilson et al [22]</b>	2018	35	male	Hodgkin lymphoma, relapsing	pembrolizumab	<b>LETM</b> (spastic tetraparesis, constipation, vomiting)	4 weeks	cc 24	LETM pons-lower thoracic spine	negative	methylprednisolone i.v.; plasma exchange	improvement
<b>Strik et al [23]</b>	2017	53	male	B-NHL	nivolumab	<b>encephalitis</b> (double vision, dysarthria, ataxia, mild cognitive dysfunction)	not clear (patient reported with delay)	cc 15, protein 0.6-0.98 g/l	small FLAIR hyperintense, contrast-enhancing lesions periventr., midbrain, brainstem	negative	methylpredn. i.v. 1g/d 5 days; IVIG 1x; cyclophosphamide 2x 750 mg	symptoms stable but disabling; assisted suicide
<b>Garcia et al [24]</b>	2018	39	female	nodular melanoma	ipilimumab	<b>meningoencephalomyelitis</b> (headache, flu-like symptoms)	7 weeks	pleocytosis	brain MRI & spinal MRI: leptomeningeal enhancement; pituitary enlargement	negative	methylpredn. 1.0 mg/kg/d i.v.	rapid improvement; relapse after 3 months IVIG/steroid refractory: Infliximab 5mg/kg i.v. 3 doses: near complete recovery
<b>Naito et al [25]</b>	2018	57	male	SCLC	nivolumab + ipilimumab	<b>acute cerebellitis</b> (nystagmus, ataxia, dysarthria)	8 weeks	cc 35, protein 0.94g/l	marked cerebellar edema, diffuse FLAIR	n.d.	2x methylpredn. 1g/d 3 days, 6 cycles plasmapheresis	limited improvement

									hyperintense cerebellar lesions		is; 2 cycles rituximab 375 mg/m2	
<b>Bot et al [26]</b>	2013	51	male	metastatic melanoma, cerebral metastasis	ipilimumab	<b>meningitis</b> (severe headache, fever)	3 weeks?	cc 20, protein 0.87 g/l	no new lesions	n.d.	dexamethasone p.o. 8 mg/d	complete recovery
<b>Martinot et al [27]</b>	2018	54	male	Hodgkin lymphoma	nivolumab	<b>PML</b> (progressive hemiparesis left)	3 weeks after last course (14 months after start)	cc 1, PCR: JCV 2230 c/ml	multiple nonenhancing lesions	n.d.	none	no improvement
<b>Matsuoka et al. [28]</b>	2018	60	male	pleomorphic lung carcinoma	nivolumab	<b>limbic encephalitis</b> (drowsiness, muscular weakness, respiratory arrest)	5 weeks	cc 16, protein 1.62 g/l, OKB pos	T2 lesions temporal lobe, thalamus, aqueduct, spinal cord	anti-Hu AB positive (before Nivo)	high dose methylprednisolone, 2x plasmapheresis	death
<b>Chaucer et al [29]</b>	2018	44	male	metastatic renal cell carcinoma + HLRCC (autosomal dominant hereditary Leiomyomatosis and Renal Cell Carcinoma)	nivolumab	<b>encephalitis</b> (deteriorated mentation, hallucinations, aggressiveness)	2 weeks	n.d.	no metastases, no other lesions	n.d.	none	improvement
<b>Patel et al. [30]</b>	2019	44	male	clear cell renal cell carcinoma	nivolumab; nivolumab + ipilimumab	non-infectious inflammatory process of the brain mimicking brain abscess	~ 9 weeks	n.d.	ring enhancing lesion in surgical cavity	n.d.	dexamethasone	complete recovery nivolumab and ipilimumab restarted 5 weeks post-admission
<b>Quach et al [31]</b>	2019	n.a.	male	metastatic melanoma	pembrolizumab	<b>meningoencephalitis</b> (headache, altered mental	~7 weeks	inflammatory changes	n.a.	n.d.	high-dose steroids	complete recovery

Author	Year	Age	Sex	Primary Disease	Treatment	Neurological Status	Duration	CSF Findings	Imaging	Other Findings	Treatment	Outcome
Zafar et al [32]	2019	59	female	laryngeal squamous cell carcinoma	nivolumab	status) + epididymo-Orchitis  <b>acute demyelinating encephalitis</b> (Nauseas, falls, weakness, altered mental status)	2 weeks	cc 74, elevated protein, OCB pos	multiple FLAIR hyperintense lesions parietal lobes + corpus callosum, Pons		methylprednisolone 1g/d 5 days, IVIG 20g/d 4 days	gradual improvement
		66	female	lung adenocarcinoma	nivolumab	<b>encephalitis</b> (right hemiballismus, dysarthria)	16 weeks	cc normal, protein 0.56 mg/dl	T2-hyperintense basal ganglia abnormalities	novel, unclassified paraneoplastic AB (CSF)	methylprednisolone 1g/d 5 days; 5 PE; IVIG 2.5g/kg, rituximab 1000 mg 1x, tetrabenazine 20 mg (3x/d)	no improvement
Shah et al [33]	2018	44	female	lung adenocarcinoma	nivolumab	<b>autoimmune encephalitis</b> (altered mental status, nausea, vomiting, seizure)	~9 weeks	cc 19, normal protein and glucose	T2 hyperintensities bilateral mesial temporal lobes + left occipital and right temporal lobe	GAD65-antibodies (CSF and serum)	methylprednisolone 1g/d 5 days; rituximab 1000 mg every 6 months	slight improvement
		78	male	malignant pleura mesothelioma	nivolumab	<b>autoimmune encephalitis</b> (fever, somnolence, INO)	3 weeks	cc 15, protein 0.9 g/l	T2 hyperintensity mesencephalon and medial thalami (day 41)	anti-Ma2 AB positive	steroids	major improvement
De la Hoz et al [35]	2019	28	female	Hodgkin lymphoma	nivolumab	<b>autoimmune encephalitis</b> (headache, nausea, dizziness)	2 weeks	cc 136, protein 0.6 g/l	inconspicuous	n.d.	methylprednisolone 1mg/kg/d	complete recovery

<b>Kopecky et al [36]</b>	2018	63	male	metastatic renal cell carcinoma	nivolumab	<b>encephalopathy</b> (change in behavior, uncontrolled movements: choreatic)	12 weeks	mild inflammatory changes	symmetrical, increased signal in basal ganglia	anti-Ma2 AB positive (CSF)	methylprednisolone 2mg/kg/d; infliximab 5mg/kg	lost to follow-up	
<b>Leitinger et al [37]</b>	2018	67	female	squamous NSCLC	nivolumab	<b>necrotizing encephalopathy</b> (disorientation, speech arrest, apraxia, seizures)	4.5 weeks	cc 30, protein 0.56 g/l	first: unremarkable; follow-up: multiple, confluent FLAIR hyperintensities	negative	IVIG 30g/d, 5 days; methylprednisolone 1g/d 2 days	no improvement, death	neuropathological: beginning necrosis both thalami, left central region
<b>Läubli et al [38]</b>	2017	53	male	lung adenocarcinoma	nivolumab	<b>cerebral vasculitis</b> (gait disturbance, speech difficulties)	not clear (soon after nivolumab initiation)	n.d.	new peritotemporal lesion	positive anti-SSA/Ro and anti-SSB/La AB	corticosteroids	improvement	histologically: necrotizing encephalitis CD8+>CD4+ T cells
<b>Choe et al [39]</b>	2016	45	female	metastatic melanoma	ipilimumab	<b>meningoencephalitis</b> (confusion, dizziness, headache, myoclonic tremor)	6 weeks	cc 53, protein 1.51 g/l	no changes	negative	dexamethasone 8mg/d, methylprednisolone 1mg/kg/d; IVIG 0.4g/kg/d 5 days	major improvement	
<b>Brown et al [40]</b>	2016	67	male	metastatic melanoma	pembrolizumab	<b>autoimmune limbic encephalitis</b> (short term memory loss, emotional lability, confusion)	~28 weeks	lymphocytic pleocytosis	T2 hyperintensity medial temporal lobes + contrast enhancement	CASPR2 AB (CSF + serum) positive	methylprednisolone i.v.	improvement	
<b>Niki et al [41]</b>	2018	51	male	squamous NSCLC	pembrolizumab	<b>autoimmune encephalitis</b> (seizures, fever, headache, gait)	24 weeks	cc 58, protein 4.46g/l	inconspicuous	negative	prednisolone 2mg/kg	improvement	



disturbances)

**Table S2.** Overview of published case-reports regarding peripheral nervous system manifestations as neurological adverse events of ICI-therapy. Besides patients' clinical data certain diagnostic findings as well as immunosuppressive.

author	year	patient age	patient sex	underlying diseases	ICI therapy	neurological symptoms	latency ICI-start/onset irAE	CSF findings	MRI	antibody findings	electrophysiology	immunosupp. therapy	outcome	additional information
Wilson et al [22]	2018	57	male	metastatic melanoma	nivolumab + ipilimumab	myasthenia gravis	4 weeks	unknown	unknown	negative		methylpredn . i.v.	rapid improvement	
Johnson et al [42]	2015	69	female	metastatic melanoma	ipilimumab	myasthenia gravis	around 10 weeks	n.d.	normal	antibodies positive (1,9 nmol/l)	decrement positive	methylpredn . i.v., plasmapheresis	improvement	
		73	female	metastatic melanoma	ipilimumab	myasthenia gravis	around 3 weeks	n.d.	n.d.	antibodies positive (13,6 nmol/l)	n.d.	high-dose corticosteroids	gradual improvement	
Sciacca et al [43]	2016	81	male	NSCLC	nivolumab	myasthenia gravis	4-5 weeks	n.d.	n.d.	antibodies 0,40 nmol/l	repetitive nerve stimulation negative; single fibre EMG of orbicularis oculi abnormal	prednisone	complete remission of MG	
Shirai et al [44]	2016	81	female	metastatic melanoma	nivolumab	myasthenia gravis	13 days	n.d.	n.d.	antibodies positive (12,4 mmol/l), others negative; CK	none	none	death	

<b>Polat et al [45]</b>	2016	65	male	NSCLC	nivolumab	<b>myasthenia gravis</b>	6 weeks	n.d.	normal	negative	normal	pyridostigmine	continued improvement	
<b>Chang et al [46]</b>	2017	75	male	metastatic bladder SCC	nivolumab	<b>myasthenia gravis</b>	3 weeks	n.d.	normal	AchR-AB positive (2,28 nmol/l), CK 1587 U/l	significant decrement	IVIG	improvement	
<b>Loochtan et al [47]</b>	2017	70	male	SCLC	ipilimumab+nivolumab	<b>myasthenia gravis</b>	16 days	n.d.	n.d.	AchR-antibodies positive (1,64 mmol/l)	decrement	prednisolone p.o.; IVIG; plasmapheresis	death (bleeding, AV-blocking)	
<b>Derle et al [48]</b>	2018	71	male	metastatic melanoma	ipilimumab	<b>myasthenic crisis</b>	1 month	n.d.	n.d.	preexisting positive AchR-antibodies	n.d.	plasma exchange, IVIG, methylpredn.	death two years later due to respiratory failure	preexisting antibody positive MG, stable for 3 years under azathioprine 100 mg/d
<b>Montes et al [49]</b>	2018	74	male	metastatic melanoma	ipilimumab	<b>myasthenia gravis</b>	6 weeks	no abnormalities	n.d.	negative	decrement positive	high-dose corticosteroids	marked improvement	
<b>Lau et al [50]</b>	2016	75	male	metastatic melanoma	pembrolizumab	exacerbation of <b>myasthenia gravis</b>	4-5 weeks	n.d.	n.d.	n.d.	n.d.	methylpredn. i.v.; IVIG	marked improvement	preexisting antibody positive MG since 4 years, stable under Aza 200 mg/d
<b>Nguyen et al [51]</b>	2017	81	male	metastatic melanoma	pembrolizumab	<b>myasthenia gravis</b>	11,5 weeks	n.d.	n.d.	negative	n.d.	prednisolone	complete	pembrolizumab was

Author	Year	Age	Sex	Primary Diagnosis	Treatment	Secondary Diagnosis	Duration	Abnormalities	Other Findings	Antibodies	EMG/NCV	Treatment	Outcome	Notes
				a									recovery	not stopped after ptosis
		86	female	metastatic melanoma	pembrolizumab	<b>myasthenia gravis</b>	6,5 weeks	no abnormalities	normal	negative	nerve conduction and repetitive stimulation normal/negative	methylprednisolone i.v.	improvement	
<b>Alnahhas et al [52]</b>	2017	84	male	metastatic melanoma	pembrolizumab	<b>myasthenia gravis</b>	3 months	n.d.	n.d.	Ach-R-antibodies positive (0,05 nmol/l)	n.d.	prednisone 60 mg/d, pyridostigmine 60 mg 1-1-1; IVIG 0,4g/kg/d 5 days	death	
<b>Zhu et al [53]</b>	2016	59	female	metastatic melanoma	pembrolizumab	<b>myasthenia gravis</b>	around 11 weeks	n.d.	normal	negative	positive decrement	prednisone, IVIG, plasmapheresis	marked improvement	history of myasthenia gravis, rheumatoid arthritis, Ach-R-AB initially positive
<b>Gonzalez et al [54]</b>	2017	71	female	metastatic uterine carcinosarcoma	pembrolizumab	<b>myasthenia gravis</b>	after fourth dose (6-9 weeks)	n.d.	n.d.	CK 1200 U/l, antibodies negative	Single fiber EMG of the frontalis muscle abnormal	pyridostigmine + prednisone	significant improvement	
<b>Cooper et al [55]</b>	2017	68	female	NSCLC	nivolumab	<b>myasthenia gravis exacerbation</b>	12 weeks	n.d.	MRI brain + spinal cord: stable to minimally decreased size of known metastatic lesions	AChR 0.28 nmol/L	repetitive nerve stimulation : significant decrements	pyridostigmine, prednisone, plasmapheresis	death	preexisting anti-AChR antibody positive ocular MG
<b>Mehta et</b>	2017	73	male	metastatic	nivolumab	<b>myasthenia</b>	18 days	no	n.d.	AchR-a		prednisolon	slight	

al [56]			female	renal cell carcinoma		<b>myasthenia gravis</b>		abnormalities		antibodies positive (8,7 mmol/l); CK 8950 U/l		pyridostigmine, IVIG, plasmapheresis	improvement	
<b>Becquart et al [57]</b>	2019	75	female	metastatic melanoma	nivolumab	<b>myasthenia gravis</b>	5 weeks	no abnormalities	brain MRI: normal	negative	normal	prostigmine	improvement	nivolumab continued for 1 more year
<b>Lara et al [58]</b>	2018	63	female	NSCLC	pembrolizumab	<b>myasthenia gravis</b>	~ 3 weeks	n.d.	brain MRI: unremarkable	highly elevated striatal muscle IgG antibody titer (1:1280).	n.d.	IVIG, high dose corticosteroid therapy, pyridostigmine	improvement	
<b>Werner et al [59]</b>	2019	62	male	metastatic melanoma	nivolumab + ipilimumab	<b>myasthenia gravis</b>	4 weeks	cc 13/ $\mu$ l	brain MRI: normal	negative	Repetitive stimulation : action potential decrement of 14% low-amplitude compound muscle action potentials (CMAP), increasing >2 after brief exercise; positive repetitive nerve stimulation	pyridostigmine, prednisone	complete recovery	
<b>Nakatan i et al [60]</b>	2018	73	female	squamous cell lung cancer	nivolumab	<b>Lambert-Eaton myasthenic syndrome</b>	20 weeks	n.d.	n.d.	anti-P/Q-type VGCC antibodies positive		pyridostigmine, ambenonium, 4-DAP	gradual improvement	

<b>Kimura et al [61]</b>	2016	80	male	metastatic melanoma	nivolumab	<b>myasthenic crisis and polymyositis</b>	2 weeks	n.d.	n.d.	AchR-antibodies positive (28 nmol/l) (before ICI: 10,2 nmol/l)	n.d.	methylpredn . i.v.; IVIG, plasma exchange	improvement	muscle biopsy: myositis
<b>March et al [62]</b>	2018	63	male	metastatic melanoma	pembrolizumab	<b>myasthenia gravis + myositis</b>	2 weeks	n.d.	normal (except for previously known metastases)	AchR-AB positive, CK 10286 U/l	n.d.	prednisone, pyridostigmine; IVIG; plasmapheresis	no improvement, death	
<b>Chen et al [63]</b>	2017	57	male	squamous cell carcinoma lung	nivolumab + ipilimumab	<b>coexisting myasthenia gravis, myositis, PNP</b>	4-6 weeks	no abnormalities	n.d.	AchR-antibody slightly elevated	axonal polyneuropathy	prednisolone i.v. + pyridostigmine	improvement, death through infection	
<b>Liao et al [64]</b>	2014	70	female	metastatic uveal melanoma	ipilimumab	<b>myasthenia gravis + myositis</b>	6 weeks	n.d.	sMRI: degenerative disease	AchR-AB positive (2,09 nmol/l), CK 1200 U/l	diffuse myopathic findings; decrement positive	methylpredn . i.v., plasmapheresis; IVIG	improvement	
<b>Tan et al [65]</b>	2017	45	male	squamous cell carcinoma lung	nivolumab	<b>myasthenic crisis + myositis</b>	2 weeks	n.d.	brain MRI: normal	Ach-R-antibodies 2,0 nmol/l	no decrement	methylpredn . i.v.; IVIG	improvement	muscle biopsy: inflammatory myopathy
<b>Huh et al [66]</b>	2018	34	female	thymic cancer (Squamous cell carcinoma)	pembrolizumab	<b>myasthenic gravis + myositis</b>	unknown	n.d.	normal	Ach-R-antibodies 0,86 nmol/l; CK 2125 U/l	normal	IVIG, methylprednisolone, prednisolone; plasmapheresis	improvement	

<b>Konoeda et al [67]</b>	2017	74	female	advanced colon cancer	nivolumab	<b>myasthenic gravis + myositis</b>	3 weeks	n.a.	n.a.	n.a.	n.a.	methylpredn . i.v.; IVIG; plasma exchange	n.a.	
<b>Kang et al [68]</b>	2018	75	male	head and neck squamous cell carcinoma	nivolumab	<b>myositis and myasthenia gravis</b>	3 weeks	n.d.	n.d.	positive AChR-antibodies, anti-striated muscle antibodies 1:320; CK 2593 U/L	n.d.	methylpredn . i.v., plasmapheresis, pyridostigmine	minimal improvement	
<b>So et al. [69]</b>	2019	55	female	metastatic melanoma	nivolumab	<b>severe myasthenia gravis + necrotizing myopathy and myocarditis</b>	2 weeks	n.d.	n.d.	positive AChR Ab (29 nmol/L), CK 13652 U/l	single-fiber electromyography: neuromuscular junction dysfunction (increased jitter)	steroid pulse, IVIG, plasma exchange	gradual improvement	AChR Ab (72 nmol/L) positive before nivolumab
<b>Moslehi et al [70]</b>	2017	65	female	metastatic melanoma	nivolumab + ipilimumab	<b>myocarditis + myositis</b>	12 days	n.d.	n.d.	antibodies n.d.; CK 17.720 U/l Trop I 51,3 ng/ml antibodies n.d.; CK 20.270 U/l,	n.d.	methylpredn . i.v.	death due to multisystem organ failure	postmortem cardiac and skeletal muscle biopsy: T-cell infiltration
		63	male	metastatic melanoma	nivolumab + ipilimumab	<b>myocarditis + myositis</b>	15 days	n.d.	n.d.		n.d.	methylpredn . i.v.; Infliximab	death due to cardiac arrest	postmortem cardiac and skeletal muscle biopsy:

Author(s)	Year	Age	Sex	Primary Disease	Treatment	Myositis Type	Duration	Abnormalities	sMRI	Antibodies	EMG	Immunosuppression	Response	Biopsy Findings
<b>Bourgeois-Vionnet et al [71]</b>	2018	79	male	metastatic lung adenocarcinoma	nivolumab	<b>myositis</b>	3 weeks	no abnormalities	unremarkable	antibodies negative; CK 2450 U/L	Single fiber EMG and repetitive nerve stimulation negative	monthly IVIGs, oral corticosteroids	marked improvement	T-cell infiltration muscle biopsy: fascicular myonecrosis, phagocytosis, perivascular inflammatory infiltrates CD8+ T-cells
<b>Fox et al [72]</b>	2016	75	female	metastatic melanoma	nivolumab	<b>myositis</b>	2-3 weeks	n.d.	n.d.	antibodies n.d.; CK 1180 U/l	n.d.	prednisone	improvement	
<b>Saini et al [73]</b>	2017	35	male	Hodgkin lymphoma	nivolumab	<b>inflammatory myositis</b>	17 weeks	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	
<b>Badovinac et al [74]</b>	2018	64	female	squamous cell lung cancer	nivolumab	<b>inflammatory myositis</b>	28 weeks	n.d.	n.d.	CK 2657 U/l; antibodies negative TPO-AB positive, ANA 1:320; others negative (TRAK, SOX,	n.d.	methylpredn . i.v.	marked improvement	muscle biopsy: inflammatory origin of muscle fibers damage
<b>Pushkar evskaya et al [75]</b>	2017	60	female	metastatic melanoma	ipilimumab	<b>ocular myositis + hypophysitis</b>	about 17 weeks	3 normal lumbar punct.	brain MRI: preexisting brain metastases	antibodies negative (TRAK, SOX,	n.d.	methylpredn . i.v., mycophenolate; IVIG	marked improvement	

Author	Year	Age	Sex	Primary Disease	Treatment	Secondary Disease	Duration	Outcome	Diagnosis	Lab	Response	Treatment	Outcome	Notes
		60	female	metastatic melanoma	ipilimumab	ocular myositis	5 weeks	n.d.	orbital MRI: thickening of right superior oblique muscle; later: all other muscles	ANA 1:320, others negative	n.d.	methylpredn . i.v., mycophenolate	marked improvement	
Lecoufle et al [76]	2013	n.a.	female	metastatic melanoma	ipilimumab	orbital myositis	around 6-9 weeks	n.d.	orbital MRI: contrast enhancement left lateral rectus muscle	negative	n.d.	high-dose steroids oral	complete recovery	
Sheik et al [77]	2015	55	female	metastatic melanoma	ipilimumab	dermatomyositis	2 weeks; relapse after 14 months	n.d.	n.d.	ANA 1:640, others negative (Jo-1.); CK 1854 U/l	n.d.	prednisone; methylpredn . i.v.	marked improvement of muscle strength	muscle biopsy: atrophy but no inflammatory myositis
Yoshioka et al [78]	2015	84	male	metastatic melanoma	nivolumab	myositis	7 weeks	n.d.	n.d.	antibodies n.d.; CK 2812 U/l	n.d.	prednisolone	complete recovery	
Vallet et al [79]	2016	86	female	metastatic melanoma	pembrolizumab	necrotic myositis	3,5 weeks	n.d.	n.d.	negative	EMG: myopathic changes	methylpredn . i.v., plasma exchange	complete recovery	muscle biopsy: multifocal necrosis, endomyosial CD8+ infiltrates
Haddox et al [80]	2017	78	male	metastatic melanoma	pembrolizumab	bulbar myopathy,	5 weeks	n.d.	sMRI: symmetric	striational	EMG: MUAP	prednisone, plasma	death	muscle biopsy:





<b>Carrera et al. [85]</b>	2017	68	male	NSCLC	tremelimumab + durvalumab	<b>myopathy involving extraocular muscles</b>	1 month	n.d.	brain MRI: normal	antibodies negative; CK 3083 U/l	EMG: complex polyphasic motor unit potentials -->inflamm at. myopathy	prednisone	improvement	muscle biopsy: infiltrat. Of endomysium and perimysium by CD4-, CD8+ cells
<b>Kadota et al. [86]</b>	2019	85	female	metastatic melanoma	nivolumab	<b>dermatomyositis</b>	4 weeks	n.d.	n.d.	negative	n.d.	prednisolone	improvement	
<b>Ogawa et al. [87]</b>	2017	88	male	metastatic melanoma	nivolumab	<b>polymyositis</b>	6 weeks	n.d.	n.d.	negative	EMG: myogenic pattern	oral prednisolone, azathioprine	death	
<b>Sekiguchi et al. [88]</b>	2019	78	male	bladder cancer	pembrolizumab	<b>myositis + diaphragm involvement</b>	2 weeks	n.d.	n.d.	AChR-AB positive 9.5 nmol/l; anti-str iational muscle antibodies positive; CK 2015 U/l	no decrement in repetitive stimulation	methylpredn . i.v., IVIG	partial improvement (limb muscle weakness recovered but respiratory function did not)	
		52	male	metastatic melanoma	nivolumab + ipilimumab	<b>GBS</b>	3-4 weeks	protein 2.3 g/l	inconspicuous	negative		IVIG	very good recovery rapid motor improvement;	
<b>Garcia et al [24]</b>	2018	55	male	melanoma IIIB	ipilimumab	<b>acute infl. demyelinating PNP</b>	6 weeks	lymphocytic pleocytosis, protein 1.75 g/l	abnormal enhancement bilat. 5th, 7th, 8th cranial nerves, cauda equina, conus normal	negative		methylpredn . i.v.	minimal paresthesia continued	
<b>Bot et al</b>	2013	63	male	metastatic	ipilimumab	<b>axonal GBS</b>	about 12	cc normal,				IVIG	died	

[26]			male	melanoma			3 weeks (3 weeks after 4th course)	protein 0.89 g/l							from respiratory insufficiency
Ong et al [89]	2018	66	male	lung adenocarcinoma	pembrolizumab	GBS	1 month		spinal MRI: only degenerative changes	negative	tibial DML prolonged, partial conduction block peroneus bilateral, sparing of sural sensory response	methylpredn . i.v.; IVIG			almost full recovery
De Maleissye et al [90]	2016	45	female	melanoma	pembrolizumab	GBS	8 weeks	slight pleocytosis, protein 0.56 g/l	normal	negative	multifocal demyelination with conduction blocks	prednisolone, IVIG			improvement
Schneiderbauer et al [91]	2017	51	male	metastatic melanoma	nivolumab	GBS	5 months	cc normal, protein 0.73 g/l	brain MRI and sMRI: normal	negative	acute demyelinating sensorimotor or PNP	methylpredn . i.v. + IVIG			nearly complete recovery
Fukumoto et al [92]	2018	66	male	metastatic NSCLC	nivolumab	acute demyelinating polyneuropathy	3 weeks	cc 4/ $\mu$ l, protein 3.4 g/l	n.d.	GM2-+ Ga1Nac-GD1a-IgM-antibodies	DML prolonged, NCV reduced	prednisolone; IVIG			improvement
Supakornnumpon et al [93]	2017	77	male	metastatic melanoma	ipilimumab + nivolumab	GBS	7 weeks	cc normal, protein 0.86 g/l	n.d.	n.d.	reduced median and ulnar cMAP amplitudes, median and ulnar conduction blocks in forearm	prednisone, IVIG			improvement
Yost et	2017	64	male	melanoma	ipilimumab +	GBS	17	cc 12/ $\mu$ l,	subtle	negative	mildly slow	IVIG,			marked

al [94]			male		pembrolizumab		months ??	protein 1.95 g/l	enhancement of facial nerves	negative	lower limb motor conduction velocities, pathological blink reflexes	prednisone p.o.	improvement
Jacob et al [95]	2016	68	female	metastatic squamous cell carcinoma lung	nivolumab	GBS	3 months	cc normal, protein 0.85 g/l	sMRI: normal	n.d.	n.d.	IVIG + plasmapheresis	death (respiratory failure)
Wilgenhof et al [96]	2011	57	female	metastatic melanoma	ipilimumab	GBS	7 weeks	cc normal, protein 1.67 g/l	brain MRI + sMRI: normal	n.d.	motor and sensory demyelinating PNP f-waves	methylpredn . i.v.	nearly complete recovery
Kelly Wu et al [97]	2017	37	female	metastatic melanoma	ipilimumab	GBS	unknown	unknown	n.d.	negative	prolonged, amplitudes smaller acute generalized motor predominant neuropathy	Droxidopa, IVIG	slight improvement
Gu et al [98]	2017	49	female	metastatic melanoma	ipilimumab + nivolumab	acute neuropathy	5 days	cc: 15/ $\mu$ l, protein 1.15 g/l	spinal MRI: normal	negative		IVIG, methylpredn . i.v.; mycophenolate + plasma exchange	mild improvement; relapse after 1 month death (hemorrhage within brain metastasis)
		81	male	metastatic melanoma (brain metastases)	pembrolizumab	acute inflammatory demyelinating PNP	4 weeks (after 2nd cycle)	albuminocytol. dissociation with elevated CSF protein	brain MRI: brain metastases	negative	consistent with motor and sensory neuropathy	methylpredn ., IVIG, plasmapheresis	
Nukui et al. [99]	2018	45	male	nasal cancer	nivolumab	acute demyelinating polyradiculoneuropathy	~ 10 weeks	cc 7/ $\mu$ l, protein 3.5 g/l	brain MRI: not remarkable; spinal MRI: gadolinium enhancement of nerve roots and cauda	negative	prolonged distal latency (DL), reduced nerve conduction velocity (NCV)	IVIG, steroid pulse therapy	improvement

		85	female	metastatic melanoma	ipilimumab + pembrolizumab	<b>CIDP</b>	20 weeks	cc normal, protein 0.74 g/l	equina normal	negative	multifocal demyelination with conduction blocks all potentials of blink response markedly delayed (demyelinating PNP)	oral and i.v. glucocorticoids, plasma exchange	no improvement	
		44	male	metastatic melanoma	ipilimumab	<b>CIDP</b>	1 week	cc normal, protein 0.44 g/l	normal (except for previously known metastases)	negative		plasmapheresis	significant improvement	
<b>Thaipisuttikul et al [100]</b>	2015	57	male	metastatic melanoma	ipilimumab	<b>peripheral neuropathy</b>	36 days	1. cc 78/ $\mu$ l, protein 0.68 g/l 2. cc 79/ $\mu$ l, protein 0.95 g/l 3. cc 8/ $\mu$ l, protein 0.32 g/l	brain MRI + sMRI: normal	negative	symetric sensorimotor or PNP	methylpredn.; infliximab; IVIG; tacrolimus + methylpredn.	slight improvement	
<b>Tanaka et al [101]</b>	2016	85	female	metastatic melanoma	nivolumab	<b>CIDP</b>	2 weeks	cc 11/ $\mu$ l, protein 3.58 g/l	brain MRI: normal; sMRI: gadolinium enhancement C7 and Th1 dorsal roots	negative	F-wave latency prolonged, conduction blocks	prednisolone; IVIG	improvement	suralis biopsy: loss of small myelinated fibres, mild lymphocytic infiltration
<b>Sepulveda et al [102]</b>	2017	44	male	metastatic melanoma	pembrolizumab	<b>motor polyradiculopathy</b>	47 weeks	cc normal, protein 0.67 g/l	brain MRI: normal; sMRI: diffuse enhancement of dorsal roots	negative	ENG: normal, EMG: reduction of number of active motor unit potentials	IVIG + oral prednisone; plasma exchange	gradual improvement	
<b>Aya et al</b>	2017	53	female	metastatic	ipilimumab;	<b>vasculitic</b>	2 weeks	n.d.	n.d.	n.d.	moderate	methylpredn	slow	preexisting

[103]			male	melanoma	pembrolizumab	neuropathy					sensory PNP	. i.v., oral prednisolone	improvement	seropositive RA; muscle biopsy: perivascular infiltration (small endoneurial vessels) of mononuclear cells
Manam et al [104]	2018	73	male	adenocarcinoma of the lung	pembrolizumab	inflammatory demyelinating PNP	3 weeks	albumino-cytol. dissociation with elevated CSF protein	n.d.	negative	n.d.	methylpredn., IVIG, plasmapheresis	gradual improvement	
Simsek et al. [105]	2018	52	male	metastatic renal cell carcinoma	nivolumab	peripheral neuropathy	10 weeks	n.d.	brain MRI and sMRI: unremarkable	CK 2440 U/l	n.d.	methylpredn. i.v.	improvement	
		62	male	metastatic melanoma	ipilimumab	peripheral neuropathy	13 weeks	n.d.	n.d.	n.d.	n.d.	methylpredn. i.v. + mycophenolate	full improvement	
Sakai et al [106]	2017	81	male	metastatic melanoma	nivolumab	mononeuropathy multiplex + rhabdomyolysis	8 days	cc 1/ $\mu$ l, protein 0.27 g/l	n.d.	negative (CK 27703 U/l)	axonal mononeuropathy multiplex	prednisolone i.v.	improvement	
Zecchini et al. [107]	2018	45	male	metastatic melanoma	ipilimumab + nivolumab, followed by nivolumab mono	Bell's palsy	2 weeks	cc 240/ $\mu$ l, protein 0.26 g/l	brain MRI: unremarkable	n.d.	n.d.	oral valacyclovir + oral prednisone	complete resolution	
Zieman et al [108]	2019	51	female	metastatic melanoma	ipilimumab + nivolumab	Bell's palsy + polyneuropathy	1 week	n.d.	brain MRI: normal	n.d.	n.d.	prednisone taper and acyclovir	improvement	
		68	female	metastatic melanoma	ipilimumab + nivolumab	Bell's palsy	about 3 weeks	n.d.	brain MRI: normal	n.d.	n.d.	prednisone taper + valacyclovir.	improvement	

<b>Jinnur et al [109]</b>	2015	66	male	metastatic melanoma	ipilimumab	<b>bilateral phrenic nerve neuropathy</b>	about 12 weeks	n.d.	sMRI normal	negative	bilateral severe phrenic nerve neuropathies	prednisone	no improvement (needed BiPAP during sleep)	
<b>Ghosn et al [110]</b>	2018	69	female	metastatic melanoma	pembrolizumab (+ T-VEC)	<b>sjögren's syndrome</b>	20 weeks	cc 92 /μl, protein 1.32 g/l,	brain MRI: enhancement of the right trigeminal Gasser's ganglia and its mandibular branch	anti-SSA elevated, other antibodies negative	absence of SNAPs in upper and lower limbs; reduced MAPs for the median and ulnar nerves	methylprednisone i.v.; IVIGs; 2nd line cyclophosphamide (replaced by rituximab)+ oral prednisone	improvement (but residuals)	biopsy of accessory salivary glands (ASGB): abnormal interstitial sclerosis with a focus of > 50 lymphocytes/4 mm <sup>2</sup> (Chisholm and Mason's score of 3 out of 4)

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