

SUPPLEMENTAL DATA

SUPPLEMENTAL TABLES

eTable1. Clinical findings in all patients tested positive for anti-CASPR2 antibodies in the Centre from January 2006 to June 2020. Data is stratified according to whether anti-CASPR2 antibodies were tested positive in cerebrospinal fluid (CSF) or in serum only.

	CSF-positive (N=48)	Serum only (N=37)	P-value
Median age (IQR)	64.5 (59, 68)	57 (44, 65)	0.005
Male sex, n (%)	47 (98)	20 (54)	<0.001
Tumor, n (%)	15 (31)	24 (65)	0.004
Thymoma, n (%)	0 (0)	17 (71)	<0.001
Anterograde amnesia, n (%)	46 (96)	0 (0)	<0.001
Seizures, n (%)	45 (94)	1 (3)	<0.001
Behavioral disorder, n (%)	42 (88)	13 (35)	<0.001
Cerebellar ataxia, n (%)	25 (52)	7 (19)	0.004
Insomnia, n (%)	27 (56)	19 (51)	0.82
Hyperkinetic movement disorder, n (%)	3 (6)	14 (38)	0.001
Motor signs of peripheral nerve hyperexcitability, n (%)	13 (27)	28 (76)	<0.001
Neuropathic pain, n (%)	15 (31)	26 (70)	0.001
Dysautonomia, n (%)	22 (46)	21 (57)	0.44
Asthenia, n (%)	34 (71)	21 (57)	0.26
Weight loss, n (%)	24 (50)	15 (41)	0.52
Axonal neuropathy, n (%)	1 (2)	2 (5)	0.82

eTable2. Demographic and tumor characteristics in 15 patients with a diagnosis of tumor.
 Abbreviations: CLL, chronic lymphocytic leukemia; N.O.S., not otherwise specified

Patient age at onset	Tumor type	Delay from encephalitis onset to tumor diagnosis (months)	Delay to follow up (months)	mRS at follow up	PNS care score
66	Prostate N.O.S.	1.0	14.8	3	4
65	Lung N.O.S.	43.0	44.0	2	3
70	Bladder N.O.S.	15.9	38.7	1	3
67	Prostate adenocarcinoma	15.0	54.6	1	3
66	Bladder N.O.S.	69.70	69.7	1	3
55	Bladder N.O.S.	66.8	82.2	4	3
60	Renal clear-cell carcinoma	26.3	62.9	0	3
64	Thyroid N.O.S.	26.7	31.5	6	3
57	Ovarian endometrioid carcinoma	-156.1	114.6	2	3
61	Oesophagus N.O.S.	29.0	29.6	6	3
65	Bladder N.O.S.	79.9	82.8	0	3
70	Lung N.O.S.	53.9	108.2	1	3
59	Thyroid papillary carcinoma	6.4	158.0	1	3
61	Prostate adenocarcinoma and CLL	5.0 and 48.9	121.2	2	3
62	Bladder urothelial carcinoma	83.8	128.8	0	3

eTable3. EEG findings in 11 patients with available EEG recordings.

	Median (range)
Routine EEG (30 minutes)	
Number of recordings, n/N (%)	40/50 (80)
Number of patients, n/N (%)	6/11 (55)
Prolonged EEG (≥ 1 hour)	
Number of recordings, n/N (%)	10/50 (20)
Number of patients, n/N (%)	5/11 (46)
Median duration, h (range)	11 (1-24)
Normal result, n (%)	6 (55)
Slow waves	
Temporal, n (%)	4 (36)
Other, n (%)	0 (0)
Generalized, n (%)	0 (0)
Interictal epileptiform discharges	
Focal, n (%)	4 (36)
Temporal	4 (36)
Other regions	0 (0)
Generalized, n (%)	0 (0)
Ictal events	
Focal onset, n (%)	4 (36)
Temporal	4 (36)
Centroparietal	1 (9)
Spread to other regions, n (%)	2 (18)
Contralateral spread, n (%)	2 (18)
Generalized, n (%)	0 (0)

eTable4. Demographic, paraclinical, and clinical features of patients according to inclusion in the cross-sectional analysis.

	Patients included in cross-sectional analysis (N=35)	Patients not included in cross-sectional analysis (N=13)	p-value
Male, n (%)	34 (97.1)	13 (100)	>0.99
Median age at onset, y, [IQR] (range)	64 [61-73] (53-82)	65 [59-67] (46-74)	0.39
Patients with tumor, n (%)	12 (34)	3 (23)	0.73
Abnormal MRI, n/N (%)	21/33 (64)	7/12 (58)	0.74
CSF, n (%)			
Normal	15 (43)	5 (39)	>0.99
Cell count > 5 cells/ μ L	13 (37)	6 (46)	0.74
Protein, g/L, median (range)	0.52 (0.2-1.38)	0.61 (0.26-1.02)	0.63
Oligoclonal bands	11/31 (36)	3/7 (43)	>0.99
Abnormal EEG, n/N (%)	20/33 (61)	8 (62)	>0.99
Serum positive for anti-CASPR2 antibodies, n (%)	35 (100)	12 (92)	0.27
Time from 1 st symptom to – days, median [IQR] (range)			
First appointment	73 [10-144] (0-822)	10.5 [5.5-72.5] (0-110)	0.31
Diagnosis	329 [165-637.5] (58-2634)	253 [120-498] (31-1164)	0.36
First immunotherapy	343 [199.5-699.5] (68-2658)	270 [153-512] (31-1162)	0.38
Peak	579 [189-761] (30-4019)	396 [179-700] (78-1856)	0.53
Last follow-up	1919 [1235-3036] (450-5675)	961 [700-2299] (320-4986)	0.066
Treatments received			
Intravenous immunoglobulins	27 (77)	10 (77)	>0.99
Steroids	21 (60)	11 (85)	0.11
Rituximab	18 (51)	8 (62)	0.53

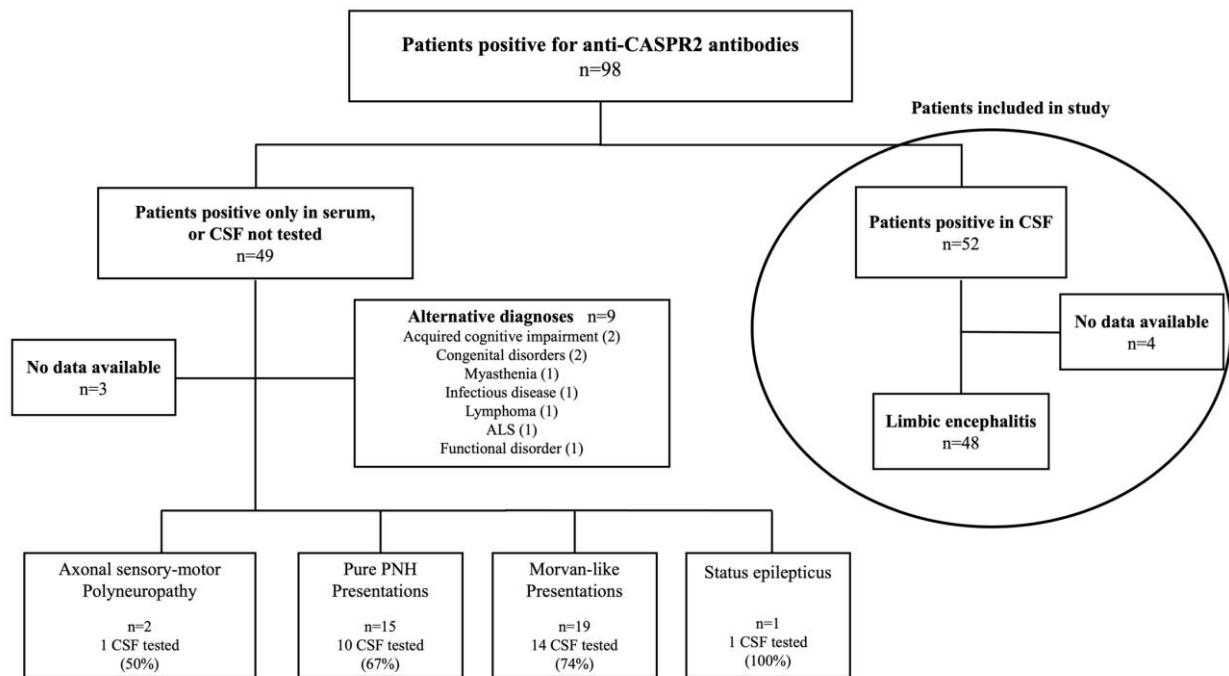
Intravenous cyclophosphamide	18 (51)	5 (39)	0.42
Plasma Exchange	2 (6)	2 (15)	0.28
Mycophenolate mofetil	2 (6)	2 (15)	0.28
Azathioprine	1 (3)	3 (23)	0.024
Methotrexate	1 (3)	0 (0)	0.54
Mitoxantrone	1 (3)	0 (0)	0.54
Symptoms at onset, n (%)			
Mood disorder	9 (26)	3 (23)	0.85
Behavioral disorder	7 (20)	3 (23)	0.82
Cognitive disorder	2 (6)	3 (23)	0.080
Cerebellar ataxia	1 (3)	4 (31)	0.005
Episodic ataxia	4 (11)	1 (8)	0.71
Seizures	12 (34)	4 (31)	0.82
Neuropathic pain	9 (26)	0 (0)	0.043
Motor signs of peripheral nerve hyperexcitability	1 (3)	1 (8)	0.46
Dysautonomia	2 (6)	1 (8)	0.80
Weight Loss	5 (14)	1 (8)	0.54
Asthenia	14 (40)	2 (15)	0.11
Insomnia	8 (23)	2 (15)	0.57
Hyperkinetic movement disorder	1 (3)	0 (0)	0.54
Symptoms at last visit, n (%)			
Mood disorder	13 (37)	8 (62)	0.13
Behavioral disorder	17 (49)	8 (62)	0.42
Cognitive disorder	22 (63)	11 (85)	0.93
Cerebellar ataxia	12 (34)	8 (62)	0.089
Episodic ataxia	5 (14)	2 (15)	0.92
Seizures	5 (14)	7 (54)	0.005
Neuropathic pain	8 (23)	2 (15)	0.57

Motor signs of peripheral nerve hyperexcitability	2 (6)	3 (23)	0.080
Dysautonomia	10 (29)	2 (15)	0.35
Weight Loss	11 (31)	3 (23)	0.57
Asthenia	15 (43)	4 (31)	0.45
Insomnia	10 (29)	5 (39)	0.51
Hyperkinetic movement disorder	1 (3)	2 (15)	0.11
Symptoms over study period, n (%)			
Mood disorder	29 (83)	11 (85)	0.73
Behavioral disorder	31 (89)	11 (85)	0.71
Cognitive disorder	33 (94)	13 (100)	0.38
Cerebellar ataxia	16 (46)	9 (69)	0.15
Episodic ataxia	17 (49)	4 (31)	0.27
Seizure	34 (97)	11 (85)	0.11
Neuropathic pain	12 (34)	3 (23)	0.46
Motor signs of peripheral nerve hyperexcitability	9 (26)	5 (39)	0.39
Dysautonomia	16 (46)	6 (46)	>0.99
Weight loss	18 (51)	6 (46)	0.75
Asthenia	25 (71)	9 (69)	0.88
Insomnia	21 (60)	6 (46)	0.39
Hyperkinetic movement disorder	1 (3)	2 (15)	0.11

SUPPLEMENTAL FIGURES

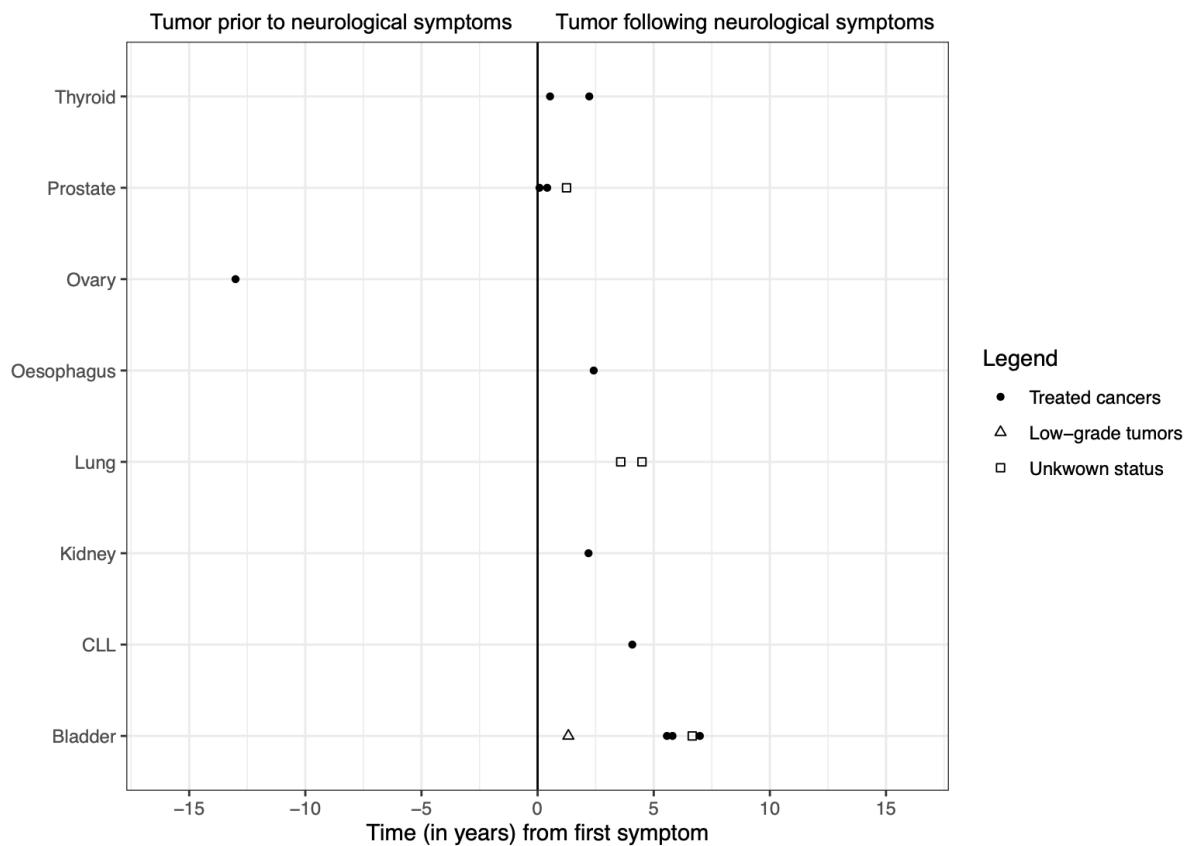
eFigure1. Flow chart featuring all patients testing positive for CASPR2 Abs, whether in CSF or only in serum.

Abbreviations: *CSF*, cerebrospinal fluid; *ALS*, amyotrophic lateral sclerosis

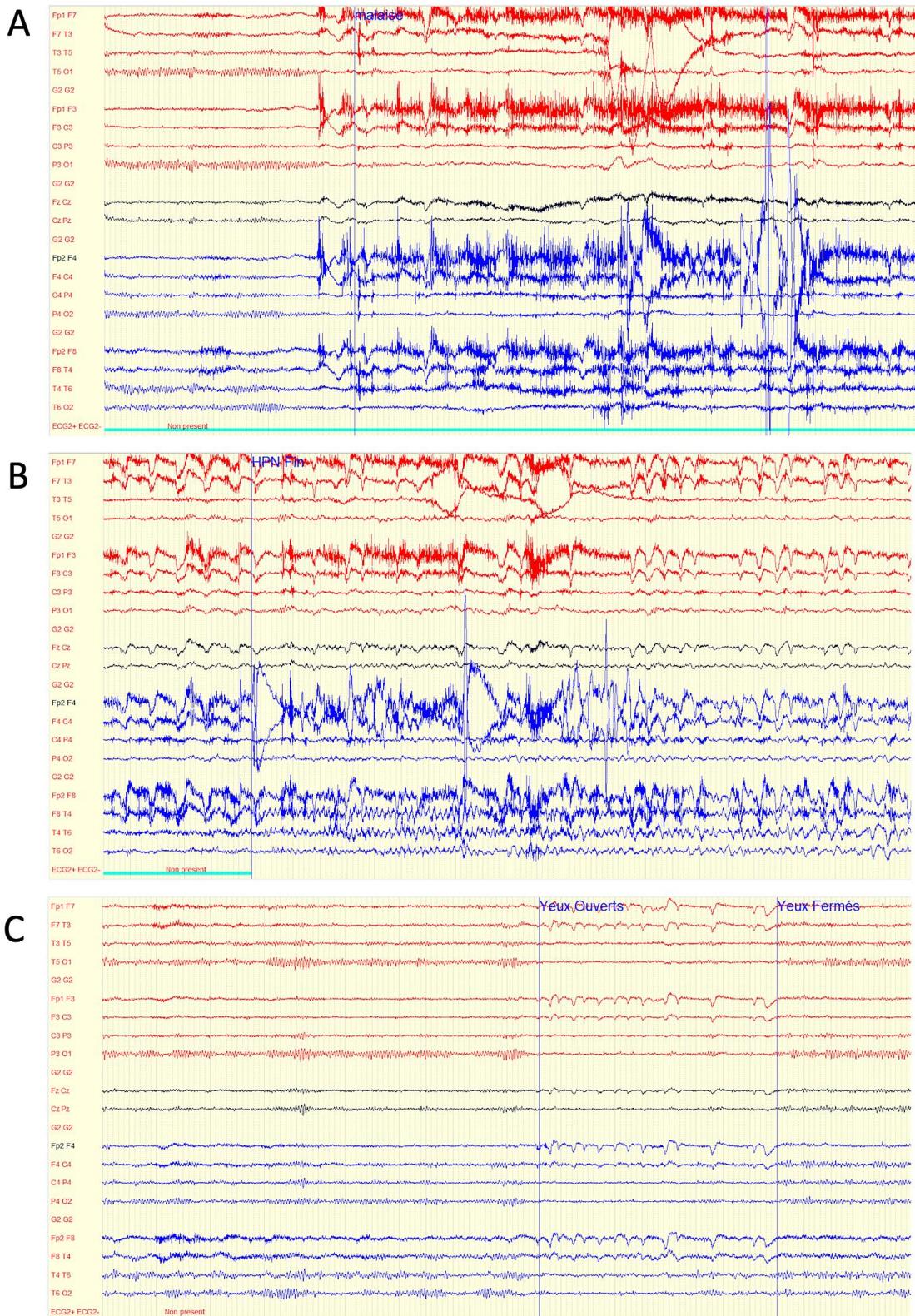


eFigure2. Timeline representation of the different tumors diagnosed in the patients, in respect with the onset of the neurologic symptoms.

Abbreviation: *CLL*, chronic lymphocytic leukemia.



eFigure3. Ictal epileptiform discharge triggered by hyperventilation during a 1-hour EEG recording in a 71-year-old male with CASPR2-encephalitis. A) 3 minutes 40 seconds after starting hyperventilation, generalized flattening over the right frontotemporal area followed by seizure onset. The patient described a sensation of anxiety, *déjà-vu*, and internal tremor. B) continuation of the seizure. C) seizure offset, followed by interictal, normal EEG with 9-10 Hz alpha rhythm attenuated by eyes opening.



eFigure4. Timeline of the occurrence of symptoms from onset to last visit, in each patient.

