eTable 1

Recruiting Centers

ITALY

1. IRCCS "G. Gaslini" Institute, Genova, Italy
2. Spedali Civili, Brescia, Italy
3. IRCCS Stella Maris, Calambrone, Pisa, Italy
4. ASST Mantova, Mantua, Italy
5. IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
6. University of Verona, Verona, Italy.
7. G. Salesi Children's Hospital, University of Ancona, , Ancona, Italy.
8. ASST Santi Paolo e Carlo, Milan, Italy.
9. Federico II University of Naples, Italy.
10. Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
11. University of Ferrara, Ferrara, IT
12. Children's Hospital Vittore Buzzi, Milan, Italy.
13. Maggiore della Carità University Hospital Novara, Italy
14. Children's Hospital A. Meyer, Florence.
15. IRCCS Policlinico San Matteo Foundation, University of Pavia, Viale Golgi 19, 27100 Pavia, Italy
16. Department of Pediatrics, Sapienza University of Rome, 00161 Rome, Italy.
17. Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

ISRAEL

18. Sheba Medical Center and Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel

CHILE

19. Clínica Integral de Epilepsia Infanto-Juvenil, Santiago, Chile

USA

20. Children's Medical Center of Dallas, Dallas, Texas, USA

eTable 2

ID [ref.]	Sex	Age (m/y)	Exam at birth	Developmental impairment onset	Epilepsy onset			Epilepsy outcome (age at seizure freedom, months)	Brain MRI (age)	Developmental outcome							STXBP1 mutation
					Age at onset (m)	Seizure type(s)	EEG at onset			Cognitive	Head control	Eye contact	Walking (age at)	Speech	Neurological examination	Behaviour	
P_1[6]	M	8 y	Normal	infancy	1.17	Focal motor (tonic-clonic), S.E.	FC SWs, diffuse slow SWs	seizure free (1.96 m)	Unremarkable	severe ID	yes	yes	yes (28 m)	no	clumsy, unsteady gate	Hyperactivity	c.704 G>A (p.Arg235Gln)
P_2[6]	M	6 y	Hypotonia, feeding difficulties	neonatal (neurological abnormalities)	0.03	focal motor (Tonic-clonic), focal non motor (dyscognitive with oral automatisms)	FC SWs, BS	seizure free from 2 -17 months of life. Relapsed	Unremarkable (2 m)	severe ID	Incomplete	yes	no	no	apostural tetraparesis (spastic); scoliosis	unremarkable	c.1216C>T (p.Arg406.Cys)
P_3[6]	F	3 y	Hypotonia, feeding difficulties	neonatal (neurological abnormalities)	2	focal motor (tonic, clonic)	BS	seizure free (6 m)	Unremarkable (4 m)	moderate delay	yes	yes	no	Few words (24 m)	abnormal	unremarkable	c.922A>T (p.Lys308X)
P_4[6]	M	23 y	Normal	infancy	0.83	Spasms	BS	active epilepsy	n.a.	severe ID	yes	yes	yes (24 m) but lost later	no	tetraplegia (spastic-dystonic)	Motor stereotypies; wake bruxism	c.1217 C>A (p.Arg406His)
P_5[6]	M	19 m	Hypotonia, feeding difficulties	neonatal (neurological abnormalities)	0.03	Focal motor (tonic-clonic), S.E.	BS	active epilepsy	supratentorial atrophy. bilateral symmetric signal changes of nucleus pallidus	severe delay	Incomplete	intermittent	no	no	n.a.	n.a.	c.1075C>T (p.Gln359X)
P_6[6]	M	10 y	Normal	early childhood	8	focal motor	multifocal SWs > FT	active epilepsy	unremarkable (8 m) ,mild atrophy (7 y)	severe delay	yes	no	yes, with assistance (20 m)	no	ataxia	Motor stereotypies (hand)	c.751G>A, (p.Ala251Thr)

P_7[6]	M	3 y	Normal	early childhood	0.1	Focal motor, focal non motor (dyscognitive with autonomic signs)	FC SWs	seizure free (8 m)	modest increase CSF spaces at the base of the brain (3 m)	mild delay	yes	yes	yes (22 m)	Short sentences (36 m)	unremarkable	unremarkable	c.430-2_430+2delinsTGGGAGA
P_8[14]	F	5.4 y	Normal	early childhood	11	focal motor (tonic, myoclonic), focal non motor (dyscognitive with oral automatisms)	SWs FT, left >	active epilepsy	FCD IB and mesial temporal sclerosis FCD IIIA (3 y)	mild delay	yes	yes	yes (17 m)	Short sentences	unremarkable	Hyperactivity	c.57_59del (p.Ile19_Lys20delinsMet)
P_9	F	8.75 y	Hypotonia	neonatal (neurological abnormalities)	0.17	focal motor (clonic)	BS	active epilepsy	unremarkable	severe ID	Incomplete	yes	no	no	Tetraparesis (flaccid)	Motor stereotypies (head)	c.1262_1262delA (pAsn422Thrfs*2)
P_10	M	3 y	Normal	neonatal (neurological abnormalities)	0.1	focal motor (tonic, clonic)	AB, MED	active epilepsy	Thin corpus callosum, bilateral frontal lobes hypotrophy	severe delay	no	no	no	no	generalized hypotonia, disarthria, hyporeflexia, ocular tremor, impaired pain sensation	unremarkable	Exones 4-5 deletion
P_11[12]	M	12 m	Hypotonia	neonatal (neurological abnormalities)	0.03	focal motor with oral automatisms	n.a.	seizure free (7 m)	n.a.	severe delay	yes	no	n.a.	n.a.	hypotonia	n.a.	c.1286T>C (p.Leu 423 Pro)
P_12	F	5 y	abnormal, not specified	neonatal (neurological abnormalities)	0.23	n.a.	n.a.	seizure free (7.5 m)	n.a.	severe delay	incomplete	intermittent	no	no	axial hypotonia, distal hypertonia	unremarkable	c. 1249G>C (p. Gly417Arg)
P_13[14]	F	4.7 y	Hypotonia	neonatal (neurological abnormalities)	1	focal motor with oral automatisms	Mildly slowed FT left>	seizure free (8 m)	modest increase CSF spaces at the base of the brain, thin corpus callosum	severe delay	incomplete	yes	no	no	Tetraparesis (spastic)	Motor stereotypies	c.1099C>Ta(p.Arg367*)
P_14	M	12 y	Normal	neonatal (neurological abnormalities)	1.33	Spasms	Hypsarrhythmia, BS	seizure free (12 m)	Mild enlargement of the lateral ventricles and periencephalic liquoral spaces (6 y)	severe ID	incomplete	yes	no	no	severe axial hypotonia, mild distal hypertonia, proximal myoclonus, sialorrhea, scoliosis	Motor stereotypies	c.1216 C>T(p.Arg406Cys)
P_15	M	4 y	abnormal	neonatal (neurological abnormalities)	0.07	Spasms	Multifocal S-SWs	Seizure free 1-2 years of life. Relapsed.	unremarkable	severe delay	Incomplete	intermittent	No	no	Axial hypotonia, distal hypertonia	unremarkable	c.1217G>A (p.Arg406His)
P_16	F	1 y	Normal	infancy	0.07	focal motor (tonic-clonic, myoclonic)	n.a.	active epilepsy	unremarkable	moderate delay	yes	yes	no	no	axial hypotonia	unremarkable	c.1057_1060del (p.Asp353Valfs*2)

P_17	M	6.75 y	Normal	early childhood	17	focal motor (tonic)	CT SW	active epilepsy	unremarkable (17 m); enlargement of the retrocerebellar spaces and peri-cerebellar CSF spaces, smaller size of the left cerebellar hemisphere (31 m); focal T2-hyperintensitie s in the subcortical white matter on temporal lobes (4 y)	moderate ID	yes	intermittent	yes (15 m)	few words	unremarkable	Motor stereotypies, Hyperactivity, autistic like	c.57_59delAAA (p.Ile19_Lys20delins Met)
P_18	M	21 y	abnormal	neonatal (neurological abnormalities)	1	focal non motor (dyscognitive with autonomic signs)	n.a.	seizure free (131 m)	unremarkable	severe ID	no	yes	no	no	Tetraplegia (spastic)	unremarkable	c.1216C>T (p.Arg406Cys)
P_19	M	2.6 y	Normal	neonatal (neurological abnormalities)	0.27	focal motor	MED	seizure free (12 m)	unremarkable	moderate delay	yes	yes	no	no	axial hypotonia	unremarkable	del 9q33.3-34.11
P_20	F	12 m	jerky movements	neonatal (neurological abnormalities)	1	focal motor (tonic), spasms	BS	active epilepsy	unremarkable (2 m)	severe delay	no	intermittent	no	no	apostural tetraparesis, nystagmus	n.a.	c.247-?_749+? (exons 5-9 deletion)
P_21	M	21 m	Normal	neonatal (neurological abnormalities)	1.67	Focal motor	AB, CT S-SWs	Seizure free 6-18 months of life. Relapsed.	Hypoplasia of corpus callosum	severe delay	Incomplete	intermittent	no	no	dyskinesias and intentional tremor	Motor stereotypies	c.993_995delGAA (p. Lys332del)
P_22	M	2.1 y	Normal	infancy	0.13	focal motor (tonic)	n.a.	seizure free (9 m)	n.a.	mild delay	yes	intermittent	yes, with assistance	no	axyal hypotonia	autistic like, bruxism	c.1702+1G>C
P_23	F	5.9 y	feeding difficulties	neonatal (neurological abnormalities)	0.47	spasms	BS	active epilepsy	thin corpus callosum, myelination delay, posterior plagiocephaly (18 m)	profound	no	no	no	no	apostural tetraparesis, erratic eye movements	abnormal	exons 5-15 duplication
P_24	M	13 m	Normal	infancy	1	spasms	MED; BS during sleep	active epilepsy	thin corpus callosum	severe delay	no	poor	no	no	quadriplegia	n.a.	c.17T>A (p.Leu6His)
P_25	M	13 y	Normal	early childhood	48	focal	n.a.	active epilepsy	unremarkable	moderate ID	yes	intermittent	yes, with assistance	few words	focal deficits; hypokinetic-rigid and dystonic features	autistic like	c.1324A>G (p.Asn442Asp)
P_26	M	4 y	Normal	early childhood	33.6	absence	polyspi ke	active epilepsy	unremarkable	severe delay	yes	intermittent	yes	no	unremarkable	autistic like	c.1216C> T (p.Arg406Cys)
P_27	F	10 y	Normal	early childhood	2.5	focal motor (tonic)	BS like; poli-spikes mediu m voltage bilatera l	seizure free (3.5 m)	unremarkable	severe ID	yes	yes	yes	no	ataxia	autistic like	c.1408G>T (p.Glu470*)

P_28	M	28 y	Normal	early childhood	72	focal motor (automatisms during sleep)	Slow waves CP, right >	active epilepsy	unremarkable	severe ID	yes	yes	yes	few words	ataxia, hypertonus	autistic like	c.1359+1G>A
P_29	F	35 y	Normal	early childhood	2	spasms	n.a.	seizure free (372 m)	unremarkable (8 y)	severe ID	yes	yes	yes	few words	ataxia, hypertonus	unremarkable	c.88-1G>C
P_30	M	29 y	Normal	neonatal (neurological abnormalities)	1.5	spasms	n.a.	active epilepsy	hypomyelination	severe ID	no	no	no	no	axial hypotonia, microcephaly	motor stereotypies (hand)	del q33.3-q34.11 (2.87 Mb)
P_31	F	4 y	Normal	infancy	0.7	spasms	hypsarrhythmia, BS	seizure free (4 m)	unremarkable (2 m)	severe delay	incomplete	intermittent	no	no	hypotonia	unremarkable	c.1095_1096del (p.Cys366Profs*13)
P_32	M	21 m	Normal	neonatal (neurological abnormalities)	0.17	spasms	BS	active epilepsy	unremarkable (1.5 m); diffuse parenchymal atrophy and lactate peak in left parietal region (11 m)	severe delay	no	no	no	no	tetraparesis (spastic-dystonic)	unremarkable	c.1461G>C (p.Glu487Asp)
P_33	M	10 m	Normal	not impaired	0.3	focal motor (clonic)	MED	seizure free (1.3 m)	Unremarkable (0.5 m)	no delay	yes	yes	n.a.	n.a.	mild hypotonia	unremarkable	c.794+2dupT
P_34	M	18 m	Normal	neonatal (neurological abnormalities)	0.5	spasms	AB, S-SWs	active epilepsy	Unremarkable (0.5 m)	profound delay	no	no	no	no	hypotonia	n.a.	c.875G>A (p.Arg292His)
P_35	F	14 y	Normal	neonatal (neurological abnormalities)	0.33	focal motor (tonic), spasms	BS	seizure free 5-10 years of age. Relapsed.	right temporal aracnoid cyst; Brain PET: right frontal low metabolism (4 y)	profound ID	no	no	no	no	severe cifoscoliosis, hypotonia	motor stereotypies (hand-oral)	c.83G>A (p.Trp28*)
P_36	M	13 y	Normal	infancy	10	focal non motor (dyscognitive)	n.a.	active epilepsy	Unremarkable (8 y)	severe ID	yes	no	no	few words	tetraparesis	aggressive (self), repetitive behaviour	c.1651 C>T (p.Arg551Cys)
P_37	F	13 m	Normal	not impaired	10	focal motor (tonic)	MED >CT	active epilepsy	Unremarkable (13 m)	no delay	yes	yes	no	no	unremarkable	unremarkable	c.1652G>A (p.Arg551His)
P_38	F	9 y	Normal	neonatal (neurological abnormalities)	0.17	focal motor (tonic), focal non motor (dyscognitive with autonomic signs)	n.a.	active epilepsy	Unremarkable (1 y)	severe ID	Incomplete	no	yes, with assistance	no	vision impaiment, microcephaly, chorea	motor stereotypies	c.420T>A (p.Tyr140*)
P_39	M	5 y	Normal	neonatal (neurological abnormalities)	0.4	focal motor (myoclonic)	BS	seizure free (0.75)	delayed myelination (3 m)	profound ID	yes	intermittent	no	no	hypotonia	autistic like	c.1217G>A (p.Arg406His)
P_40	M	19 y	Normal	early childhood	5	n.a.	n.a.	active epilepsy	Unremarkable	severe ID	yes	intermittent	yes	no	hypotonia	autistic like	c.128-130del (p.Ser43del)
P_41	M	4 y	Normal	infancy	0.63	focal motor (tonic, myoclonic)	n.a.	seizure free 3 months - 2.5 years. Relapsed	Unremarkable	severe delay	yes	intermittent	no	no	hypotonia	motor stereotypies, bruxism	c.578+1G>A (exon 8 GT donor)
P_42	M	4 y	Normal	infancy	0.67	focal motor (tonic, myoclonic)	n.a.	seizure free 3 months - 4 years. Relapsed	Unremarkable	severe delay	yes	intermittent	no	no	hypotonia	motor stereotypies	c.578+1G>A (exon 8 GT donor)

P_43	M	5 y	Normal	infancy	16	focal motor (myoclonic), generalized (tonic-clonic) with fever	n.a.	active epilepsy	Unremarkable	severe delay	yes	no	yes	no	unremarkable	motor stereotypies	c. 1652G>T (p.Arg551Leu)
P_44	M	18 y	Normal	infancy	0.33	spasms	BS	active epilepsy	Unremarkable (3 m)	Severe ID	yes	yes	no	no	Hyperlaxitud, central hypotonia, hypereflexia.	motor stereotypies	c.1162C>T (p.Arg388*)
P_45	F	4 y	Normal	infancy	1	n.a.	Hypsarrhythmia	seizure free (24 m)	n.a.	severe delay	Yes	Yes	No	no	Hyperlaxitud, central hypotonia, hypereflexia.	motor stereotypies	c.875G>A (p.Arg292His)
P_46	F	13 y	Normal	early childhood	9	focal motor with oral automatisms, generalized (clonic)	n.a.	active epilepsy	mild asymmetry temporal pole (left < right), mild cortical thickening left fusiform gyrus (11 y)	moderate ID	yes	yes	yes (18 m)	yes (11 m)	unremarkable	oppositive, provocative, irritable	c.596G>A (p.Arg190Gln)
P_47	F	10 y	hypotonia, feeding difficulties, hyporeactivity	neonatal (neurological abnormalities)	2	spasms, focal motor (clonic)	BS	seizure free (3 m)	hypomielination, thin corpus callosum (5 y)	severe ID	yes	no	no	no	quadriplegia, choreoathetotic movements	autistic like	del 9q33.3-34.11 (2.4 Mb)
P_48	F	18 y	Normal	neonatal (neurological abnormalities)	6	focal motor with impaired awareness	AB	active epilepsy	thin corpus callosum, microcephaly (11 y)	severe ID	yes	no	yes, with assistance	no	dyspraxia, intentional myoclonus, distal inferior limb hypertonia	autistic like	c.416C>T (p.Pro139Leu)

Legend: AB, abnormal background (slow); BS, burst-suppression; CP, centro-parietal; CT, centro-temporal; FC, fronto-central; FT, fronto-temporal; ID, intellectual disability; m, months; MED, multifocal epileptiform discharges; SW, spike-waves; y, years