TABLE S1. SUMMARY OF STUDIES

Author and year (N=Number of patients)	Setting and time period	Type of study	Age in months	Sex	Dose and duration (treatment protocol)	Additional details	Definition of resolution	Probability of resolution of infantile spasms [and hypsarrhythmia]*
ADRENOCORTICOTROPIC HORMONE (ACTH)								
Hrachovy et al, 1983 [1] (N=12)	Single center study at Houston, TX Period not specified, study published in 1983	Double-blind placebo-controlled study	Range: 3.5-24	Not specified	IM natural ACTH 20 IU/day	No prior treatment with ACTH or steroids	Spasm cessation and resolution of hypsarrhythmia at 2 weeks after treatment initiation	Clinical: 7/12 (0.5833) [Clinical + hypsarrhythmia: 7/12 (0.5833)]
Snead et al, 1989 [2] (N=15)	Single center study at Birmingham, AL, USA 1984-1985	Prospective open trial	Mean: 7.5 Range: 2-18	M: 8 (53%) F: 7 (47%)	IM natural ACTH 150 IU/m^2/day	7 patients had other treatments at the time of ACTH	No spasms and normal EEG at 14 days	Clinical: 12/15 (0.8000) [Clinical + hypsarrhythmia: 12/15 (0.8000)]
Baram et al, 1996 [3] (N=15)	Single center study at Children's Hospital of Los Angeles, CA, USA Period not specified, study published in 1996	Randomized single-blinded study of IM ACTH high dose versus oral prednisone	Median (p_{25}-p_{75}): 5 (3-6)	M: 4 (27%) F: 11 (73%)	IM natural ACTH 150 IU/m^2/day	2 patients had TSC	Spasm resolution 14 days after treatment initiation and resolution of hypsarrhythmia on EEG including a full sleep-wake cycle	Clinical: 14/15 (0.9333) [Clinical + hypsarrhythmia: 13/15 (0.8667)]
Vigevano & Cilio, 1997 [4] (N=19)	Single center study at Rome, Italy 1992-1995	Randomized not blinded clinical trial (followed by a cross-over phase)	Mean (range): 5.3 (2-9)	M: 7 (37%) F: 12 (63%)	IM synthetic ACTH 10 IU once a day	1 patient discontinued ACTH because of side effects	Spasm resolution 14 days from treatment initiation	Clinical: 14/19 (0.7368) [Clinical + hypsarrhythmia: 14/19 (0.7368)]
Yanagaki et al, 1999 [5] (N=13)	Single center study at Tokyo, Japan 1991-1997	Randomized controlled trial high-dose versus low-dose ACTH	Mean (SD): Cryptogenic 5.8±2.6 Symptomatic 7.4±3.3	M; 8 (62%) F; 5 (39%)	IM synthetic ACTH 0.025 mg/Kg/day	Excluded patients previously treated with ACTH, corticosteroids, or intravenous immunoglobulin	Spasm resolution and disappearance of the hypsarrhythmia pattern within 2 weeks of treatment initiation	Clinical: 11/13 (0.8462) [Clinical + hypsarrhythmia: 11/13 (0.8462)]
Lux et al, 2004 [6] (N=25)	Multicenter study in the UK 1999-2002	Randomized non-blinded clinical trial	Median (p25-p75): 5 (3.5-7)	M: 14 (56%) F: 11 (44%)	IM synthetic ACTH 0.5-0.75 mg every other day	Excluded patients with diagnosis or suspicion of TSC; 2 patients allocated to ACTH	Reported spasm resolution for at least 48 hours including day 13 and 14 of treatment	Clinical: 19/25 (0.7600) [Clinical + hypsarrhythmia: 16/18 (0.8889)]

						received prednisolone 4 patients received lower dose due to adverse effects		
Lin et al, 2006 [7] (N=53)	Single-center study at National Taiwan University Hospital 1987-1998	Retrospective study	Age at spasm onset: Mean (SD): 8.2 (1.2) Age at treatment: Mean (SD): 11.1 (1.4)	M: 25 (47%) F: 28 (53%)	IM synthetic ACTH 2.5 IU/Kg/day	Excluded patients treated with ACTH or steroids before. Every patient received a three-day trial of 30-50 mg/Kg/day pyridoxine before ACTH was administered. 7 patients had TSC	Cessation of spasms and dissappearance of hypsarrhythmia at 2 weeks	Clinical: 46/53 (0.8679) [Clinical + hypsarrhythmia: 46/53 (0.8679)]
Kossoff et al, 2008 [8] (N=20)	Single-center study at Johns Hopkins, Baltimore, MD 1996-2007	Retrospective study	Age at treatment: Median (p25-p75): 6.6 (5.9-7.9)	M: 13 (65%) F: 7 (35%)	IM natural ACTH 150 IU/m^2/day for 1 week and ACTH 75 IU/m^2/day for the second week	Inclusion of patients with other seizures prior to spasms unless they used an ASM for spasms	Complete absence of visible spasms by the family for at least a 24 hour period within the first 14 days after treatment	Clinical: 17/20 (0.8500) [Clinical + hypsarrhythmia: 12/15 (0.8000)]
Cohen-Sadan et al, 2009 [9] (N=14)	Multicenter study in Israel 1985-2002	Multicenter retrospective study	Mean: 5 Range: 2-6.5	M: 9 (64%) F: 5 (36%)	IM natural ACTH 100 IU every other day or ACTH 20-40 IU every day	Patients with no abnormalities on MRI, normal metabolic work-up, no history of hypoxic-ischemic encephalopathy, and normal development prior to onset of spasms	Resolution of spasms at 2 weeks	Clinical: 11/14 (0.7857) [Clinical + hypsarrhythmia: 12/14 (0.8571)]
Wanigasinghe et al, 2015 [10] (N=49)	Single center study at Colombo, Sri Lanka 2010-2014	Single-center single-blind randomized trial	Mean (SD): 9.9 (8.7)	M: 31 (63%) F: 18 (37%)	IM synthetic ACTH 40-60 IU/every other day	13/49 patients had prior treatment with ASMs	Spasm freedom for at least 48 hours at day 14	Clinical: 18/49 (0.3674) [Clinical + hypsarrhythmia: 9/49 (0.1837)]
Knupp et al, 2016 [11] (N=97)	Multicenter study in the USA 2012-2014	Prospective cohort study	Median: 6	M: 54 (56%) F: 43 (44%)	IM natural ACTH 150 IU/m^2/day (recommended dose)	Included patients with different etiologies, including TSC	Absence of spasms at 2 weeks from treatment initiation	Clinical: 66/97 (0.6804) [Clinical + hypsarrhythmia: 53/97]

Hodgeman et al, 2016 [12] (N=57)	Single-center study at Boston Children's Hospital, Boston, MA 2011-2015	Retrospective review	Median (p25-p75) age at onset: 6 (4.8-8.3) Median (p25-p75) delay to treatment: 16 (7-50) days	M: 25 (44%) F: 32 (56%)	IM natural ACTH 150 IU/m^2	12 patients had prior treatments	Absence of spasms at day 14	Clinical: 40/57 (0.7018) [Clinical + hypsarrhythmia: 40/57 (0.7018)]
Yin et al, 2017 [13] (N=111)	Single-center study at Xiangya Hospital, Changsha, China 2010-2016	Retrospective review	Age of onset: Mean: 5.9 SD: 4.4	M: 69 (62%) F; 42 (38%)	IM natural ACTH 2-4 IU/Kg/day (maximum 40 IU/day)	Excluded patients with a prior use of hormonal treatments	Absence of spasms at day 14	Clinical: 52/111 (0.4685) [Clinical + hypsarrhythmia: 46/111 (0.4144)]
Gowda et al, 2019 [14] (N=18)	Single center study at Indira Gandhi Institute of Child Health, Bangalore, India 2013-2015	Single-center prospective non-blinded randomized trial	Age of onset: Mean: 8.6 SD: 6.3 Age of treatment: Mean: 9.4 SD: 5.3	M: 12 (67%) F: 6 (33%)	IM natural ACTH 100 IU/m^2/day	No prior steroids	Absence of reported spasms at least 48 hours including days 13 and 14.	Clinical: 9/18 (0.5000) [Clinical + hypsarrhythmia: 7/18]
Dressler et al, 2019 [15] (N=16) **[USED ONLY FOR THE ANALSYSIS OF CLINICAL AND EEG RESOLUTION OF SPASMS]**	Single center study at Vienna, Austria 2008-2017	Randomized controlled trial of ACTH versus ketogenic diet	Median: 6	M: 10 (63%) F: 6 (38%)	IM synthetic ACTH 150 IU/m^2/day	Excluded patients with prior treatment with ketogenic diet or steroids	Spasm resolution and dissappearance of the hypsarrhythmia at day 28 from treatment initiation	Clinical: 11/16 (0.6875) [Clinical + hypsarrhythmia: 11/16 (0.6875)]
PREDNISONE OR PREDNISOLONE								
Hrachovy et al, 1983 [1] (N=12) [LOW DOSE]	Single center study at Houston, TX	Double-blind placebo-controlled study	Range: 3.5-24	Not specified	Oral prednisone 2 mg/Kg/day	No prior treatment with ACTH or steroids	Spasm cessation and resolution of hypsarrhythmia at 2 weeks after treatment initiation	Clinical: 5/12 (0.4167) [Clinical + hypsarrhythmia: 5/12 (0.4167)]
Baram et al, 1996 [3] (N=14) [LOW DOSE]	Single center study at Children's Hospital of Los Angeles, CA, USA	Randomized single-blinded study of im ACHT high dose versus oral prednisone	Median (p_{25}-p_{75}): 7 (5-8.75)	M: 8 (57%) F: 6 (43%)	Oral prednisone 2 mg/Kg/day	2 patients had TSC	Spasm resolution 14 days after treatment initiation and resolution of hypsarrhythmia on EEG including a full sleep-wake cycle	Clinical: 4/14 (0.2857) [Clinical + hypsarrhythmia: 4/14 (0.2857)]
Lux et al, 2004 [6] (N=30)	Multicenter study in the UK	Randomized non-blinded clinical trial	Median (p_{25}-p_{75}): 5 (4-6)	M: 18 (60%)	Oral prednisolon	Excluded patients with diagnosis or	Reported spasm resolution for at least 48 hours	Clinical: 21/30 (0.7000)

	1999-2002			F: 12 (40%)	e 40-60mg/day	suspicion of TSC 5 patients received lower dose due to adverse effects	including day 13 and 14 of treatment	[Clinical + hypsarrhythmia: 10/14 (0.7143)]
Ware et al, 2012 [16] (N=17)	Single center study at Melbourne, Victoria, Australia 2007-2009	Single-center retrospective review	In the whole study of 28 infants Range: 3-14	In the whole study of 28 infants M: 17 (61%) F: 11 (39%)	Oral prednisolone 40-60mg/day	New-onset epileptic spasms	Absence of spasms at 2 weeks No patients with TSC in this group	Clinical: 13/17 (0.7647) [Clinical + hypsarrhythmia: unknown]
Adhami & Harini, 2013 [17] (N=7)	Two center study at University of Massachusetts Medical Center and Boston Children's Hospital, Boston, MA 2011-2013	Two-center retrospective review	Age of treatment: Median (p_{25}-p_{75}): 7.5 (6.9-9.3)	M: 2 (29%) F: 5 (71%)	Oral prednisolone minimum 4 mg/Kg/day (maximum 60 mg/day)		Absence of spasms on day 14	Clinical: 7/7 (1) [Clinical + hypsarrhythmia: 7/7 (1)]
Chellamuthu et al, 2014 [18] (N=32) [LOW DOSE]	Single center study at New Delhi, India 2012-2013	Single-center prospective randomized open-label trial	Median (p_{25}-p_{75}): 10.5 (8-14.5)	M: 23 (72%) F: 9 (28%)	Oral prednisolone 2 mg/Kg/day	No patients with TSC	Spasm freedom for at least 48 hours at day 14	Clinical: 8/32 (0.2500) [Clinical + hypsarrhythmia: 7/32 (0.2188)]
Chellamuthu et al, 2014 [18] (N=31) [HIGH DOSE]	Single center study at New Delhi, India 2012-2013	Single-center prospective randomized open-label trial	Median (p_{25}-p_{75}): 12 (9-18)	M: 21 (68%) F: 10 (32%)	Oral prednisolone 4 mg/Kg/day	No patients with TSC	Spasm freedom for at least 48 hours at day 14	Clinical: 16/31 (0.5161) [Clinical + hypsarrhythmia: 12/30 (0.4000)]
Wanigasinghe et al, 2015 [10] (N=48)	Single center study at Colombo, Sri Lanka 2010-2014	Single-center single-blind randomized trial	Mean (SD): 8.3 (6.2)	M: 25 (52%) F: 23 (48%)	Oral prednisolone 40-60mg/day	12/48 patients had prior treatment with ASMs	Spasm freedom for at least 48 hours at day 14	Clinical: 28/48 (0.5833) [Clinical + hypsarrhythmia: 21/48 (0.4375)]
Yi et al, 2015 [19] (N=20)	Single center study at Jiangxi Children's Hospital, Nanchang, Jiangxi province, China 2011-2012	Single-center descriptive retrospective study	Mean: 16.5 Range: 3-53 Age of onset: Mean: 8.9 Range: 2.6-32	M: 17 (85%) F: 3 (15%)	Oral prednisone 40mg/day	No patients with TSC 6 patients had received at least two ASMs prior to prednisone	Absence of spasms at 2 weeks	Clinical: 16/20 (0.8000) [Clinical + hypsarrhythmia: 12/20 (0.6000)]
Knupp et al, 2016 [11] (N=54)	Multicenter study in the USA 2012-2014	Prospective cohort study	Median: 7	M: 26 (48%) F: 28 (52%)	Oral corticosteroids: Prednisolon	Included patients with different etiologies,	Absence of spasms at 2 weeks from	Clinical: 30/54 (0.5556)

					e 40mg/day (recommended dose)	including TSC	treatment initiation	[Clinical + hypsarrhythmia: 21/54]
Gonzalez-Giraldo et al, 2018 [20] (N=87) **First 15 patients also reported in Kossoff et al, 2009 [21]**	Single center study at Johns Hopkins Hospital, Baltimore, MD, USA 2006-2016	Single-center retrospective review	Age of onset: Median: 6 Range: 1-32	M: 49 (56%) F: 38 (44%)	Oral prednisolone 40-60 mg/day	Prednisolone was the first treatment or the second treatment after failure of 2 weeks of ketogenic diet	Absence of spasms and absence of hypsarrhythmia at 2 weeks	Clinical: 62/87 (0.7126) [Clinical + hypsarrhythmia: 56/87 (0.6437)]
Eliyan et al, 2019 [22] (N=102) **First 27 patients also reported in Hussain et al, 2014 [23]**	Single center study at Mattel Children's Hospital, Los Angeles, CA 2009-2017	Single-center retrospective review	Age of onset: Median (p_{25}-p_{75}): 7.1 (4.9-12.1)	M: 61 (60%) F: 41 (40%)	Oral prednisolone 8 mg/Kg/day with a maximum of 60 mg/day	5 patients had TSC Prior treatment with short or low-dose treatment with prednisolone or ACTH in 12 patients. Prior treatment with VGB in 36 patients	Absence of spasms and absence of hypsarrhythmia (with overnight EEG) at 2 weeks and no recurrence of spasms over 28 days	Clinical: 60/102 (0.5882) [Clinical + hypsarrhythmia: 60/102 (0.5882)]
Yi et al, 2019 [24] (N=39)	Single center study at Jiangxi Children's Hospital, Nanchang, Jiangxi province, China 2015-2016	Single-center prospective randomized trial comparing prednisone with prednisone and topiramate	Age of onset: Median: 6 Range: 2-39 Age of treatment: Median: 9.2 Range: 3.5-40	M: 26 (67%) F: 13 (33%)	Oral prednisone 40mg/day (increased to 60mg/day if spasms sustained by day 7)	No prior hormone therapy 1/39 (3%) patient had TSC	Absence of spasms for at least 48 hours at 2 weeks	Clinical: 28/39 (0.7180) [Clinical + hypsarrhythmia: 21/39 (0.5385)]
Gowda et al, 2019 [14] (N=15)	Single center study at Indira Gandhi Institute of Child Health, Bangalore, India 2013-2015	Single-center prospective non-blinded randomized trial	Age of onset: Mean: 6 SD: 5.2 Age of treatment: Mean (SD): 13.9 (9.2)	M: 9 (60%) F: 6 (40%)	Oral prednisolone 4mg/Kg/day (maximum 60mg/day)	No prior steroids	Absence of reported spasms at least 48 hours including days 13 and 14.	Clinical: 5/15 (0.3333) [Clinical + hypsarrhythmia: 4/15 (0.2667)]

***The definition and follow-up time for clinical resolution of spasms is quite consistent between studies. In contrast, the definition and follow-up time for resolution of hypsarrhythmia is highly variable between studies as explained at (https://ivansanchezfernandez.github.io/CE_InfantileSpasms/Hypsarrhythmia.pdf.**

Data in rows marked as [LOW DOSE] and in rows marked as [CLINICAL OUTCOME AT 28 DAYS] were not used for the main analysis as explained in the main text. When there were

several doses used for ACTH in the same study (low and high dose), we only considered data from the high dose ACTH.

Legend: ACTH: Adrenocorticotropic hormone. **ASM:** Anti-seizure medication. **EEG:** Electroencephalogram. **F:** Female. **IM:** Intramuscular. **IU:** International units. **Kg:** Kilogram. **M:** Male. **mg:** milligram. **MRI:** Magnetic resonance imaging. **SD:** Standard deviation. **TSC:** Tuberous sclerosis complex. **UK:** United Kingdom. **USA:** United States of America. **VGB:** Vigabatrin.

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